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A TREATISE

ON

CHOLELITHIASIS.

BY

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TRANSLATED BY

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Dedicated

TO

Dr. ADOLF KUSSMAUL,

Professor in the Kaiser Wilhelm's University, Grosshezogl, Badischen Geheimrath,

On February 22nd, 1892,

In the name of the Medical Faculty of the Kaiser Wilhelm's University in Strassburg,

BY

B. NAUNYN.

PREFACE.

It was the wish of the faculty that some public testimony of our attachment to you, our honoured colleague, should be offered on this occasion, and it fills me with lively satisfaction that I have been deputed to offer it.

The treatise which I have the honour of dedicating to you is linked with your name by more than one tie. The investigations upon which it is based have been carried out in the Strassburg Clinic, over which you presided for twelve years. There I found many diagnostic and therapeutic traditions, handed down from your time, which have afforded me food for reflection, and quickly convinced me that my subject, cholelithiasis, is one in which you also have taken a special interest.

I venture to hope, therefore, that this tribute of respect, presented to the veteran master by his successor, will not prove unwelcome.

NAUNYN.

Strassburg, *February 22nd*, 1892.

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CHOLELITHIASIS.

CHAPTER I.

Form, Structure, and Composition of Gall-stones.

1. *Classification of Gall-stones.*

The following principal classes of gall-stones may be distinguished:—

1. *Pure cholesterin stones.*—These are hard; usually of oval or roughly spherical form, and seldom exhibiting facetting; of the size of a cherry to that of a pigeon's egg. They are pure white, or yellowish, and translucent, or more rarely brown, greenish, or brownish-black on the surface. The surface is as a rule smooth or nodular; rarely there is a crystalline coating, and more rarely still, crystals which have their origin in the deeper layers penetrate to and appear upon the surface. On section stratification is absent, or only feebly marked, the substance being white and crystalline throughout, or showing brown deposits between the crystals, especially in the centre. On fracture a radiating crystalline striation is distinctly visible.

2. *Laminated cholesterin stones.*—These are for the most part hard, but occasionally when dry they are brittle and friable. The surface is of various tints—white, grey, yellow, green, brown, or brownish-black. In form and size they resemble pure cholesterin stones, but are more often distinctly facetted. In section they are more or less distinctly laminated, the laminæ varying greatly in thickness (from 0·1 or less to 1 millimeter) and in tint. Layers which are almost purely white alternate with others which are yellow, brown, and even green or red. The external layers are often not crystalline, but vitreous or earthy. The nearer the centre is approached the more crystalline is the structure. Very frequently the central portion is differentiated from the laminated crust by its distinctly crystalline or lobulated

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structure, so that a nucleus is present, clearly marked off from the surrounding portions. Yet this delimitation is by no means complete, and even with the naked eye it can be seen that crystals originating in the nucleus penetrate the layers of the crust, radiating outwards through them. On fracture this radiating structure is often clearly brought out, even in stones which exhibit distinct lamination when seen in section.

The cholesterin nuclei here alluded to, which, as we shall see later, are of secondary origin, must be distinguished from included nuclei.

Of the stones of these two classes (1 and 2), those of the first kind consist of nearly pure cholesterin, and those of the second kind consist for the most part, up to as much as 90 per cent., of that substance. The more obvious the crystalline structure the more does this constituent preponderate ; but even the coloured and earthy layers consist for the most part of cholesterin. In addition to this there are present as constant constituents, but in these stones only in comparatively insignificant quantities, bilirubin-calcium in the brown, and biliverdin-calcium in the green laminæ, whilst in the green layers there is almost always much calcium carbonate in addition.

3. *The common gall bladder stones.*—The great bulk of gall-stones are included in this category. Such stones are of very various sizes and forms, and their surfaces differ much in tint. For the most part they are distinctly facetted, and one recognizes at once that they have been pressed and squeezed against each other, for it is to this that they owe their form. Their surface is usually yellow, but often brown or white ; in size they seldom equal a large cherry, and much more frequently they do not reach such dimensions, being often no larger than a pin's head or even smaller. When freshly removed from the gall bladder they are often, but not always, still soft, so that they can be crushed into a greasy crumbling pulp. When dried they become harder and undergo general shrinkage, often without developing any noteworthy fissures or cracks.

When cut with a knife or saw they present a harder, and often a quite hard, crust, usually distinctly laminated. The nucleus may be still soft and greasy, and only in exceptional instances is it already as firm as the crust. Within the nucleus there is frequently a cavity, situated in the centre, of irregular cavernous

outline, and filled with a yellowish alkaline liquid. Occasionally this cavity is large in proportion, so as to include the greater part of the calculus, and it may even involve the laminated crust.*

Such calculi never exhibit any distinct crystalline structure to the naked eye.

4. *Mixed bilirubin-calcium calculi.*—Such stones are usually as large as a cherry or larger, and lie singly, or at most in groups of three or four, in the gall bladder or large bile ducts. Their form is determined by the situation in which they lie, and when multiple they exhibit pressure surfaces (facetting).

They consist entirely, or with the exception of a nucleus of proportionately quite insignificant dimensions, of concentric layers of a reddish-brown or dark-brown material (the layers being much thicker than those met with in laminated cholesterin calculi), which is seldom quite hard, and which contracts on drying, often with the formation of fissures or cracks. The outer layers flake off, or the entire stone breaks up into broken fragments of its concentric envelopes. Towards the centre the layers frequently appear paler, firmer, and coarsely crystalline, so that a sharply-defined cholesterin nucleus presents itself.

Even the external laminæ of such bilirubin-calcium stones often contain much cholesterin, and even when they are dark brown or dark reddish-brown in colour as much as 25 per cent. of this substance may be present in them. The remainder consists of bilirubin-calcium, with small quantities of copper, probably also in combination with bilirubin, and varying amounts, usually mere traces, of iron.

5. *Pure bilirubin-calcium calculi.*—These stones are never large ; they vary from the size of a grain of sand to that of a pea, and rarely exceed these dimensions. They occur in two distinct forms. Those of the first type are solid brownish-black concretions, quite small (of the size of a pin's head or larger), with rough irregular surfaces. They are for the most part of wax-like consistency, and occasionally show a tendency to became welded together, so that the larger ones may consist of small granules which have thus become fused. On drying

* The cavity in the centre of gall-stones has been previously described by Simon, Meckel, and Hein.

they shrink considerably, and often break up into small particles during the process.

Those of the second type are harder, but still, as a rule, are only of small size, from that of a grain of sand to that of a pea: they have very various forms, and often exhibit processes. The surface of the larger and even of the slightly distorted specimens is smooth. Their colour is steel grey or black, with a pronounced metallic lustre, which is especially conspicuous in the crumbled or pounded material. They are firm, hard, brittle, but I have never found the larger specimens homogeneous; but they consist of a spongy structure, in the meshes of which lie small granules with a metallic lustre, such as are also met with loose in the neighbourhood of such larger concretions.

These tiny calculi, whichever form they assume, consist almost exclusively of the calcium compounds of bilirubin and its higher oxidation products, free bilirubin and free biliverdin being only present in traces. Bilirubin-calcium is, as a rule, the chief constituent, but there are always present, and often in quantity, biliverdin-calcium and bulifuscin. Bilicyanin is rarely present, bilihumin, on the other hand, practically always. The last-named substance often forms a chief constituent, and in one case, in which it was in part combined with lime, it constituted more than 60 per cent. of the entire mass of a calculus.

These stones contain only quite minute quantities of cholesterin, and sometimes mere traces, which are difficult of detection.

6. *Rarer forms.*

(a) *Amorphous and incompletely crystalline cholesterin gravel.* —Small calculi varying from the size of a grain of sand to that of a large pea, which are often exactly like pearls, from their subdued lustre both on the surface and in section. In their centre there is always a nucleus of different structure, and I have often found within them small black stones of bilirubin-calcium, whilst in some there is only an admixture of bilirubin-calcium which imparts a brown colour to the central portion. They seldom show lamination. To the naked eye they never exhibit a definitely crystalline structure, and under the microscope they appear vitreous or exhibit incipient crystallization of cholesterin from the centre outwards. With the

exception of the foreign nucleus, which has been somehow enclosed, such stones consist of pure cholesterin.

(b) *Calcareous stones.*—Apart from that which is combined with bilirubin, I have met with lime in fairly large amount in gall-stones in the form of simple carbonate.

Calcium carbonate occurs in many calculi. Frerichs describes a large gall-stone which was covered externally with a calcareous crust, and I have very frequently found irregular spheres and lumps of calcium carbonate in the nuclei of the common gall-stones. The same substance is also specially apt to be present in the crusts of such calculi as exhibit a bright green colour; here it is either distributed between the layers of cholesterin in spherical or granular masses, or it penetrates the crust in a columnar form from the surface right down to the nucleus.

Even in small laminated stones of a pure brown colour and rich in bilirubin-calcium, I have often found much calcium carbonate, and in these it was distributed between the laminæ and in the nucleus, in the form of the above-mentioned spherical particles.

Stones consisting mainly of calcium carbonate are of very rare occurrence. In two such cases there were present in the gall bladder of a corpse numerous calculi of this kind, all of about the same size. In one instance the stones were completely covered with spines, were dark brown in colour and somewhat flattened, in the other they were smooth. In both instances they presented in their interior a system of cavities, like the passages made by a shipworm, which penetrated the entire calculus, and in these were contained (the stones became dry in my hand) a powdery mass which consisted of a little cholesterin, bilirubin-calcium, biliverdin-calcium, and bilihumin.

Although calcium carbonate calculi may differ so widely in appearance, they are always easily recognizable by their great hardness. One can frequently notice this on merely scratching the concretion with the finger-nail and much more obviously on cutting it with a saw.

(c) *Concretions with included bodies and conglomerate stones.*— Gall-stones not infrequently have a nucleus which can be quite clearly recognized as an independent calculus. For example, we

may find a pure cholesterin stone constituting the nucleus of a concretion, the thick crust of which has throughout the consistence of a bilirubin-calcium stone ; or a small black bilirubincalcium calculus may be met with as the kernel of a cholesterin stone, &c.

In many instances two or more small calculi are welded together into a conglomerate by means of a cortex shared in common.

I myself have never seen foreign bodies forming the nuclei of gall-stones, but such occurrences have been repeatedly recorded by earlier observers. Lobstein, for example, found a round worm as the nucleus of a concretion ; Bouisson, a portion of a distoma hepaticum; Naucke, a needle ; and Frerichs, a plumstone.

(d) *Casts of bile ducts.*—In cattle tubular casts of the larger bile ducts are not infrequently present. They consist of pure bilirubin-calcium. Among human subjects such casts are very rare ; but, on the other hand, among the small, brittle bilirubincalcium calculi there are always some which are hollow, and which are actually casts of the smaller biliary ducts. In the case of a patient with leucocythæmia, who had no jaundice, I found in the common duct a remarkable cast-like stone, which consisted of almost pure and finely crystalline cholesterin.

2. *Situation, and its Influence upon the Form of Gall-stones.*

Pure bilirubin-calcium stones are not only found in the gall bladder (and here occasionally in the mucous membrane), but are also frequently met with in the intrahepatic ducts. The true denizens of the gall bladder are the common mixed cholesterin stones. These are almost exclusively confined to this situation, and here always occur—I can find no better short expression for it—gregariously. Occasionally they have been removed from the gall bladder in thousands, and I myself once found in a single gall bladder 5,000 such stones, varying from the size of a millet-seed to that of a hazel-nut. It is a very noteworthy fact that, as Hein was the first to point out, the stones of this kind removed from any one gall bladder are always alike in appearance and constitution.

Large gall-stones, whether cholesterin calculi (Nos. 1 and 2)

or large mixed bilirubin-calcium stones, are usually found in
the gall bladder, but, often too, in the cystic and common ducts.
They lie in a recess of the gall bladder or in the ducts, closely
embraced by their walls, either singly or in a closely-packed
group of two or three. Sometimes the mucous membrane is
adherent to their surface, and may even be bound down to it by
fibrous bands. Much less commonly such stones lie free in the
gall bladder, and if this be full, swimming in the bile ; under
such circumstances they may exhibit projecting crystals upon their
surfaces. In the much commoner cases in which the stone is
closely embraced by the mucous membrane its surface is, as a
rule, rough or granular. The form of these large calculi is
adapted to that of the cavities in which they lie. Facets are
only present when several lie closely packed together, and even
then are but slightly developed on such large stones. On the
gregarious stones of the gall bladder, on the other hand, facets
are, as is well known, usually present. They are seldom wanting
on the calculi of medium size, which are, on the one hand, wont
to be present in sufficient numbers in the gall bladder, and, on
the other hand, on account of their size, are not easily rolled
about within it. On the small stones there are often no facets,
because such calculi, even when present in sufficient numbers,
are easily rolled to and fro.

With very few exceptions the facetting of the concretions
is due to their having been pressed against each other whilst
still soft. There can be no doubt of this fact, which rests upon
evidence of various kinds. It is easily proved in the case of
laminated stones by the fact that the superficial laminæ are not
removed over the flattened areas, as would be the case if we
were dealing with abraded surfaces, but are continued without
interruption over the whole of the flattened surfaces ; moreover
they frequently show signs of having been compressed in these
parts, appearing narrower, often firmer, and, in the case of
coloured layers, more deeply pigmented than in the remaining
portions which have not been subjected to pressure.

Such pressure effects are met with in calculi which have
become quite hard and no longer compressible by such forces
as here come into play. Such stones, too, must have been soft
at some earlier period.

Facets unquestionably produced by the friction of calculi

against each other are certainly very rare. I myself have never met with such. In cases which I have thought to be of this nature, section of the stone has always shown that one was dealing with pressure surfaces. On the other hand, the angles and corners of a stone are sometimes abraded to a certain extent.

(e) *The chemical constituents of gall-stones.*—Cholesterin and bilirubin-calcium are the most important chemical constituents of gall-stones. Calcium carbonate ranks next to these, but it is only in rare instances that it determines the structure of the concretions.

In association with bilirubin-calcium the higher oxidation products of the bile pigment, biliverdin, bilicyanin, bilifuscin, and bilihumin are occasionally present, usually in the form of calcium compounds. Copper, probably as bilirubin-copper, and iron are almost always mixed with the bilirubin-calcium, both in very minute quantities, amounting to about a tenth part of the mass of lime.

Occasionally other inorganic constituents are also present. Thus Frerichs describes biliary concretions (which I myself have also had an opportunity of examining) consisting of the calcium compounds of the bile pigments, and contained globules of metallic mercury. Now and then admixtures of calcium sulphate or phosphate are met with, constituents which have no important share in the structure of such concretions in general. Stress must be laid upon the fact that free bilirubin is not included among the constituents of gall-stones.

In testing the stones for free bilirubin, chloroform which is absolutely free from acid must of course be employed for its extraction, and it is better that it should have been allowed to stand over caustic lime. Under these conditions one never obtains more than minute traces of free bilirubin.

The salts of the bile acids, again, are only met with in traces in fully formed calculi.* The small quantities of these substances present really appertain to bile which has soaked into the stone.

* Frerichs quotes analyses of several calculi of extraordinary composition. Among which was one of a gall-stone from an ox containing abundance of the alkali salts of the bile acids. My statement, above, that the cholates are absent from the concretions refers only to human gall-stones ; and, moreover, the stone of which Frerichs gives the analysis differs completely, according to his own description, from the ordinary gall-stones of oxen.

CHAPTER II.

The amount of the stone-forming substances, viz., cholesterin and lime, present in the bile is independent of the general metabolism and of diet. Both substances are derived from the mucous membrane of the biliary passages.

Biliary concretions consist, as has already been sufficiently stated, chiefly of cholesterin and bilirubin-calcium. It is therefore necessary to study, first of all, as fully as possible, the secretion of cholesterin and of lime in the bile.

1. *Cholesterin Secretion in the Bile.*

Cholesterin is, as has been long known, a constant constituent of the bile of human beings and of many of the mammalia. It is, however, extremely widely distributed in the animal and vegetable kingdoms, and is met with not only in the bile, but also in many normal and living tissues, as well as in many that are diseased and necrotic.

In animals it occurs most abundantly in the brain, spinal cord, and peripheral nerves, and next to these in the yelk of egg, semen, and both in the corpuscles and serum of blood ; in human milk, in sweat and in the fleeces of sheep, in the vernix caseosa, in the intestinal contents and meconium. Pohl extracted it from urine to the amount of 2·5 per mille, and identified it by the sulphuric acid and iodine, and nitric acid and ammonia reactions. The urine was that of an epileptic who had taken as much as 23 grammes of bromide of potassium in a day. Moreover, cholesterin is very frequently present in organs which have undergone fatty changes, *e.g.*, spleen, kidneys, testicles ; in ovarian and thyroid cysts ; in the fatty detritus of atheromatous foci in the arterial walls ; in serous exudations ; in pus ; in tubercular and necrotic masses ; in carcinomata and sarcomata ; and in especially large quantities in cholesteatomata. In the vegetable kingdom also it is very widely distributed, as Benecke and Ritthausen have shown.

From this it is evident *a priori* that there are many and various possible sources of the cholesterin of the bile. It is

possible that the liver excretes it from the blood, or that it is formed as a specific secretion-product of the liver, or it may be produced there or in the bile passages independently of the special hepatic functions.

Many authors accept the view that the cholesterin is excreted in the liver from the blood. The earlier Strasburg school sought, in their time, to establish this view by experimental investigations, which had nevertheless lapsed into oblivion in company with Austin Flint's doctrine of cholesterinæmia.

Of recent years a number of investigations, originating from my clinic in Strasburg, have dealt with this question.

Jankau endeavoured to ascertain definitely whether the administration of cholesterin increased the amount of that substance present in the bile. He worked with rabbits with temporary, and with dogs with permanent, biliary fistulæ. He administered to the animals large quantities of cholesterin* dissolved in oil or in lipanin, in some instances by the stomach or bowel, and in others by subcutaneous injection. In the cases in which it was introduced into the stomach or bowel it was proved by quantitative estimation of the cholesterin in the contents of the stomach or bowel that it was for the most part absorbed. After subcutaneous injection the autopsy showed that the injected cholesterin solution had disappeared.

The estimation of the cholesterin was done according to the process recommended by Hoppe-Seyler in his " Anleitung."

The results of Jankau's experiments are embodied in the following table :—

TABLE I.—RABBITS.

Weight of the rabbit in kilos.	Method of experimentation.	Time allowed for secretion, in hours.	Amount of bile secreted in c.c.	Solid constituents			Amount used in experiments in c.c.	Cholesterin			Hourly secretion.
				No. of c.c. of bile.	Amount found in grammes.	Per cent.		Amount found in grammes.	Per cent.	Percentage of solid residue.	
2	2 grms. cholesterin in lipanin, by the mouth.	6	31	½	0·0553	1·38	26	0·004	0·016	1·16	0·0008
1½	1 grm. subcutaneously	6	71	3	0·0550	1·83	19	0·007	0·035	1·91	0·004
1½	Ditto	6	55	3	0·0482	1·60	38	0·008	0·021	1·31	0·002
2	1 grm. in duodenum...............	6	40	4	0·0660	1·66	35	0·005	0·015	0·09	0·001
2	5·5 grms. by the mouth	6	32	5	0·091	1·82	27	0·007	0·026	1·42	0·001

* The cholesterin obtained from Merk, of Darmstadt, was stated by him to have been derived from the blood and brains of animals.

The amount of cholesterin in the normal fistula bile of rabbits was estimated by Jankau as from 0·9—1·5 per cent. of the solid constituents, so that there was here no increase.

TABLE II.—DOGS.

Method of experimenting	Period of secretion in hours.	Amount secreted in c.c.	Solid constituents. Amount found in grammes.	Per cent.	Bile examined in c.c.	Cholesterin. Amount found in grammes.	Per cent.	Percentage of solid constituents.	Per hour.	Remarks.
Cholesterin 0·5 grm. by the mouth.	6	28	3	0·138	4·6	25	0·011	0·044	0·978	0·002	The administrations were always at 11 and 2 o'clock. The period of collection always commenced at 11 o'clock.
Ditto 1·0 ditto	6	19	3	0·168	5·6	16	0·013	0·084	1·5	0·002	
Ditto 2·0 ditto	7	28	3	0·159	5·3	25	0·011	0·044	0·978	0·002	
Following day	3	11	1	0·151	5·6	10	0·0024	0·024	0·470	0·001	
Cholesterin 1·0 grm. subcutem.	7	23	3	0·162	5·4	20	0·011	0·055	1·019	0·002	
Following day	2	13	1	0·054	5·5	12	0·0044	0·040	0·72	0·004	

Seeing that the normal amount of cholesterin in the fistula bile of dogs is about 1 per cent. of the solid constituents, here again there was no increase.

The percentage of cholesterin in the solid constituents of the bile should be constant, but the differences between the individual figures are not inconsiderable.   These differences should, perhaps, be ascribed in part to shortcomings of the method, which, when we are dealing with such small quantities of cholesterin as are contained in fistula bile of rabbits and dogs, must have an important influence.   At any rate no noteworthy increase of cholesterin in the bile occurs after the administration of cholesterin, and of eleven experiments on dogs and rabbits one only yielded an amount of cholesterin, which rose considerably above the normal, reaching 1·8 per cent.

It seems to me, then, that it follows from Jankau's experiments that no excretion whatever of cholesterin from the blood takes place in the bile.

Complementary to Jankau's experiments are others by Thomas, which show that the amount of cholesterin in the bile is not dependent upon diet.

Here, as with Jankau's results, the great fluctuations of the

cholesterin contents of the bile are to be noted. However, in whatever way the reckoning be made, the figures certainly do not show that the amount of cholesterin contained in the bile is influenced, to any degree worth mentioning, by any particular diet. On the other hand, there occurred in one instance an undoubted rise of the contained cholesterin when the dog became ill, and, moreover, the dependence of the amount of fat in the bile upon the character of the diet was very obvious. These two facts seem to be to increase the significance of the negative result above referred to.

TABLE III.

Nature of tha Diet.	Quantity collected in hours.	Percentage of dry residue therein.	Estimated quantities for 100 c.c. of liquid bile.		Estimated quantities for 100 grms. dry residue.		Means of excreted quantities of cholesterin in grammes per hour.	Remarks.
			Fats.	Choles-terin.	Fats.	Choles-terin.		
Meat	52 in 3	5·14	0·082	0·04	1·47	0·9	0·0073	
Meat	44 ,, 2½	4·69	0·09	0·022	1·9	0·48	0·0033	
Meat	50 ,, 3	4·38	0·071	0·03	1·62	0·68	0·0005	
Series A. (1) Fat and Bread	15 ,, 2	7·0	0·262	0·065	3·75	0·93	0·0049	
Series B. (1 and 3) {Fat and Bread	23 ,, 2½	6·98	0·182	0·057	3·595	0·82	0·0052	
Fat and Bread	59 ,, 6¾	6·92	0·311	0·051	4·49	0·74	0·0044	
Series C. {Olive Oil ...	35·5 ,, 3	6·86	0·24	0·05	3·51	0·77	0·0059	
Fat and Bread	41·5 ,, 5	7·07	0·25	0·048	3·53	0·69	0·0039	
Olive Oil ...	59·5 ,, 6	9·59	0·413	0·055	4·30	0·58	0·0055	
Series D. {Fat and Bread	40 ,, 3	8·26	0·279	0·06	3·379	0·73	0·008	
Fat and Bread	58 ,, 5	8·39	0·36	0·057	4·29	0·68	0·006	
Olive Oil ...	46·5 ,, 6	6·70	0·408	0·038	6·03	0·57	0·0029	
Meat	92 ,, 6	3·95	0·261	0·047	6·6	1·19	0·0072	
Series A. (2 and 3) {Fat and Bread	20 ,, 3	5·73	0·19	0·082	3·29	1·43	0·0054	Dog ill; severe catarrh of biliary passages.
Fat and Bread	15 ,, 3	6·03	0·135	0·146	3·24	2·42	0·0109	
Series C. Fat and Bread	16 ,, 2	6·80	0·33	0·114	4·89	1·67	0·0091	

I also instigated some investigations into the amount of cholesterin in human bile in various diseases, which were carried out by Kausch and published in his thesis.

No increase of biliary cholesterin appeared to exist in any of

the diseases investigated by Kausch, and it is only, as a rule, when concretions are present in the bile that this secretion is very rich in cholesterin. Taking them as a whole it appears from the investigations of Jankau, Thomas, and Kausch that the cholesterin-content of the bile is independent of the administration of cholesterin and of the amount of this substance in the blood; that the most wide differences of diet are also without effect upon it, and that even in the majority of diseases it undergoes no noteworthy alteration. These conclusions are certainly of great importance in connection with the ætiology of gallstones, and will have to be further discussed in this connection. For our present purpose they appear to me to point to the conclusion that the cholesterin of the bile is neither a product of general metabolism nor a specific secretion product of the liver.

This suggests the idea that it is derived from the mucous membrane of the bile passages, for the secretion from diseased mucous membranes constantly contains cholesterin, and often in no less quantities than bile itself.

TABLE IV.

	Percentages contained in sputum.		Percentages contained in the solid residue.	
	Cholesterin.	Fat.	Cholesterin.	Fat.
Sputum in catarrhal bronchitis ...	0·09	0·6	2·2	12·8
Sputum in putrid bronchitis ...	0·15	—	2·0	—

Cholesterin is present in pus, according to an exhaustive analysis by Robin, even to the amount of 7 per cent. of the solid constituents.

A comparison between the bile and the sputum and pus which were analyzed may appear at first not to be permissible, since, leaving pus aside, these sputa came from mucous membranes which were the seats of inflammation, and in which an abnormally great amount of degeneration and shedding of epithelium was taking place. Yet it is by no means improbable that an active shedding of epithelial cells from the mucous membrane of the biliary passages goes on even under normal conditions, and that,

as a consequence, products of tissue destruction are mixed with normal bile; since the bile is undoubtedly an active poison for protoplasm, and some of the epithelial cells of the mucous membrane must continually succumb to the injurious action of the deleterious liquid.

I am not at present in a position to bring forward any further proof of the origin here suggested of the cholesterin present in bile. One certainly not infrequently finds that normal dog's bile which has long been stagnant in the gall bladder contains an amount of cholesterin which, in proportion to the total solid constituents, is markedly greater than that of fistula bile; and this seems to lend countenance to the view that the bile, when in contact for a long time with the mucous membrane of the gall bladder, undergoes a further impregnation with cholesterin. Yet, in the first place, this result is by no means constant, and, in the second place, the relation between the several solid constituents of the bile undergoes much alteration during a long sojourn in the gall bladder, as the result of unequal absorption of its various components.

In giving my adhesion to the view that the cholesterin is derived from the epithelium of the biliary passages, I do not, of course, mean to assert that the hepatic cells do not in like manner yield cholesterin to the bile; but the occasional formation of cholesterin by the destruction of liver cells cannot be regarded as a specific secretion by the liver.

2. *The Secretion of Lime in the Bile.*

It is a point on which definite information is desirable, whether and to what extent the administration of lime in the food increases the amount of lime in the bile, since in many quarters the view, which was first maintained by Bramson, is still firmly held, that the increase of lime salts in the bile due to a diet rich in lime, and especially to hard drinking-water, gives rise to the production of precipitates of bilirubin-calcium therein, and thus leads to the formation of concretions.

Generally speaking, no increase of lime in the bile is obtained by the administration of lime in the food. This is shown by the following experiments which were carried out by Jankau.

Table V.

Period of secretion Date	Time	Period of secretion in hours.	Amount of secretion in c.c.	Reaction of the bile.	Specific gravity of bile.	Solid constituents — Amount of bile taken in c.c.	Amount of solids in grammes.	Percentage.	Amount used in experiment in c.c.	Quantity found in grammes.	Calcium sulphate — Percentage in liquid bile.	Percentage in solid constituents.	Amount in bile secreted.	Lime — Percentage in liquid bile.	Percentage in solid constituents.	Bile.	Hourly amounts — Solid constituents.	Approximate amount of lime.	Feeding times.	Nature of food.
March 28, 29, 29	3.30—6.30, 10.30—1, 3.30—4	6	103	Neutral	1016	3	0·148	4·93	100	0·0595	0·050	1·215	0·017	0·017	0·357	17·16	0·8408	0·00290	March 27, at 10.30 a.m. ... 27, „ 2 p.m. ...	At each 1 lb. meat and 10 grms. calcium carbonate.
March 30, 31, 31	3.30—6.15, 10.45—12.30, 3—5	6¼	167	Neutral	1017	3	0·171	5·7	164	0·0750	0·0457	0·8	0·022	0·013	0·235	25·69	1·4643	0·00354	28, „ 10 a.m. ... 28, „ 3 p.m. ... 29, „ 10 a.m. ... 30, „ 10 „ ...	At each 1 lb. meat and 10 grms. calcium carbonate. 1 lb. meat and 15 grms. calcium carbonate. 1 lb. meat and 10 grms. neutral calcium phosphate.
April 3, 4	4—6, 10.30—6	9½	156	Neutral	1017	3	0·130	4·3	153	0·0850	0·0540	1·255	0·025	0·016	0·367	16·10	0·6923	0·00255	30, „ 3 p.m. ... 31, „ 10 a.m. ... 31, „ 3 p.m. ...	1 lb. meat and 15 grms. calcium phosphate. As on preceding day.
April 5, 6, 6	3—6, 11—1, 3—5.30	7½	80	Alk. ...	1018	3	0·126	4·2	77	0·0380	0·0490	1·166	0·011	0·014	0·343	10·60	0·4452	0·00148	April 1 „ ... 2 „ ... 3, at 10 a.m. ...	At each 2 lbs. meat. 1 lb. meat and 15 grms. calcium lactate.
April 7, 7	11—2, 2.45—5.30	5¾	110	Alk. ...	1018	3	0·152	5·06	107	0·0530	0·0490	0·962	0·016	0·014	0·283	19·13	0·9092	0·00268	3, „ 3 p.m. ... 4, „ 10 a.m. ...	Same as last meal. 1 lb. meat and 40 grms. calcium lactate.
April 8, 8, 10	11—1, 3—5, 3.30—6.45	7¼	120	Alk. ...	1016	3	0·125	4·17	100	0·0600	0·0600	1·441	0·017	0·017	0·424	16·55	0·6901	0·00261	4, „ 3 p.m. ... 5, morning ... 5, noon ... 6—11 inclusive ...	Same as last meal. Mixed food. 1 lb. meat. At each meal 2 lbs. meat. The animal refused water.

Moreover, the trifling amount of lime contained in bile is, at any rate in part, secreted by the mucous membrane of the biliary passages,* for the mucus secreted by mucous membranes always contains lime. On the other hand, it cannot be demonstrated that lime salts are actually present in the bile in the liver itself. Lastly, it must be expressly stated that the fistula bile of human beings as well as of dogs contains lime, and that here again no distinct increase of lime in bile from the gall bladder can be conclusively demonstrated.

* Frerichs has already expressed this view, which he bases upon observations on gall-stones.

CHAPTER III.

On the Solution of the Calculus-forming Substances in the Bile.

The calculus-forming substances, cholesterin and bilirubin-calcium, are both insoluble in water.

1. Cholesterin is held in solution in the bile chiefly through the instrumentality of the bile salts of the alkali metals and the soaps and fats. Table VI., which was constructed by Happel from the results of his own experiments, shows the solubility of cholesterin in these substances.

Table VI.

Solubility of cholesterin in various media at 37°—38° C. :—

Name of solvent.					Amount of cholesterin soluble in 100 c.c.	
Olein	...	...	...	...	5	grms.
Medicinal soap	...	...	2·5 per cent.		0·9	,,
,,	,,	...	1	,,	0·7	,,
,,	,,	...	0·5	,,	0·4	,,
,,	,,	...	0·25	,,	0·1	,,
Sodium glycocholate	...	2·5	,,	0·17	,,
,,	,,	...	1	,,	0·1	,,
,,	,,	...	0·5	,,	0·07	,,
,,	,,	...	0·25	,,	0·03	,,
Sodium taurocholate	...	2·5	,,	0·18	,,
,,	,,	...	1	,,	0·1	,,
,,	,,	...	0·5	,,	0·08	,,
,,	,,	...	0·25	,,	0·05	,,

In all instances the cholesterin was allowed to stand in contact with the solvent for 24—36 hours at the temperature mentioned.

It is seen that at about 37° C. glycocholate and taurocholate of sodium in 0·25—2·5 per cent. solutions dissolve about a tenth part of their own mass of cholesterin. Soap in equally dilute solutions dissolves about half its own mass of cholesterin. Fat (olein) dissolves 5 per cent. of cholesterin. According to all analyses of bile—I refer to those published by Kausch in his dissertation—

human bile contains ten times, or even more than ten times, as much alkaline bile salts as cholesterin. There are also to be considered the fats and soaps which as a rule are present in bile in quantities many times, and often as much as ten times, greater than that of cholesterin.

The solution of cholesterin in the bile is not interfered with by its concentration, and one can evaporate down the bile of dogs and human beings, even to dryness, without ever seeing any separation out of cholesterin, even after long standing. Seifert, and after him Thudichum, have attached importance to the ease with which glycocholic acid is split up into glycochol and cholalic acid, believing that in this way the power of the alkaline bile salts to dissolve cholesterin is impaired.

But by such an occasional decomposition of glycocholic acid the conditions for the solution of cholesterin will not be very materially altered, seeing that, according to Dr. Minkowski's estimations, the cholesterin will, under such circumstances, be nearly half as freely dissolved as by the glycocholate itself; and, taking into account the soaps and fats, sufficient solvent material for the cholesterin will still be present. Moreover, the conclusion that, as a result of the breaking up of glycocholic acid, cholesterin is precipitated from the bile is not, so far as I am aware, supported by any proof. I have never known this substance to be precipitated as the result of the onset of decomposition, even when it was present in great abundance. Neither can it be shown that precipitation of cholesterin from the bile results from deficiency of its solvents, at any rate at the body temperature (38° C.). In the bile from human corpses one certainly often finds cholesterin separated in glistening crystals, and this although the bile contains sufficient glycocholate and fats to hold in solution, at the body temperature, the whole of the cholesterin present, including that which has crystallized out. Under these conditions the separation has taken place from the cooling of the bile *post-mortem*.

However, I do not, of course, wish to state that the cholesterin *cannot* crystallize out of the bile of living human beings, although it contains a sufficiency of solvents. There is always the possibility of such an occurrence, even when the solution is still far from saturation, if only a suitable focus of crystallization be provided. The part which such crystallisation out from

the bile actually plays in the growth of gall-stones will be seen later.

2. *Bilirubin-calcium.*—The bile always contains bilirubin and lime, and yet the bile of dogs and human subjects can be concentrated, and even evaporated to dryness, redissolved and again concentrated, without the production of a precipitate of bilirubin-calcium being obtained, provided decomposition be excluded; and yet under such conditions bilirubin itself often separates out, and that in large quantities.   In the same way one often finds in the completely inspissated bile in the normal gall bladders of dogs bulky precipitates of bilirubin, but not of bilirubin-calcium.

One can extract abundance of bilirubin from human or dogs' bile by means of neutral chloroform, even when the bile has a neutral or alkaline reaction, as has been already stated by Hoppe-Seyler and others.   If one adds to such bile, not too rich in bilirubin, lime-water (or even a solution of calcium carbonate in water containing carbonic acid), no bilirubin-calcium is at first precipitated, even when so much lime is added that bilirubin can be no longer extracted with neutral chloroform.*   One can often add in this way to bile an equal bulk of lime-water without the appearance of anything more than a slight grey turbidity.   On long standing this turbidity subsides as a scanty precipitate of usually quite colourless, or rarely of pale yellow-tinted, calcium carbonate.   Further addition of lime-water leads eventually to a precipitation of bilirubin-calcium, and then almost the whole of the bilirubin promptly comes down in the form of this compound.

In bile which is very rich in bilirubin this precipitation of bilirubin-calcium takes place sooner, but even then only after the addition of considerable quantities, about an equal bulk, of lime-water, and is then always almost complete.   There are, however, substances present in the bile which are capable of hindering such precipitation, even in the face of a conspicuous increase of the amount of lime present.

The alkaline bile salts possess this power.   It was only necessary to add a few drops of lime-water to a faintly ammoniacal solution of bilirubin of a saturated dark brown colour to precipitate the bilirubin, but from a $2\frac{1}{2}$ per cent. solution of sodium glycocholate, which was similarly coloured by dissolved bilirubin, precipitation only took place on the addition of five times its volume of lime-water.

The calcium combines at first with the glycocholic acid; at any rate one sees, on cautiously adding the lime-water, that where it mixes with

* Even when, as often happens, the original bile contained no bilirubin which could be extracted with neutral chloroform, no bilirubin-calcium is precipitated on the addition of small quantities of lime-water.

the bilirubin solution a dense colourless precipitate at first forms, which redissolves on shaking. Exactly the same thing happens on the addition of a not too concentrated solution of calcium chloride; and here also the calcium salt of the bile acid is first formed. When one allows the calcium chloride solution to fall in drop by drop, a grey precipitate forms, which dissolves on shaking, and in this way one can add a considerable quantity of lime before the permanent precipitate of calcium glycocholate carries down the bilirubin with it. Nevertheless, the solution of sodium glycocholate does not by any means behave in this manner towards all calcium salts. Thus, when a saturated solution of calcium carbonate in carbonic acid is added in about equal volume to a concentrated solution of bilirubin in ammonia, which is as nearly as possible neutral, after about 24 hours standing in an open vessel bilirubin-calcium is precipitated, even when the solution contains 1—2 per cent. of bile salts. This precipitate of bilirubin is usually attended by simultaneous separation of calcium carbonate.

Possibly bilirubin-calcium is only precipitated when the solution has a certain definite reaction. Certainly it is not thrown down from acid solutions, even when the previously alkaline bile has been rendered acid by leading carbonic acid through it. It is equally certain that a somewhat strongly alkaline reaction, due to a quite trifling excess of ammonia, suffices to hinder its precipitation.

In the experiments quoted the reaction of a solution of calcium carbonate in carbonic acid is at first acid; but by the evaporation of the carbonic acid it gradually becomes neutral and ultimately alkaline. It is possible that at a certain definite moment the reaction is reached which favours the separating out of bilirubin-calcium.

Steinman has found that egg albumen precipitates calcium carbonate from solutions of calcium salts. Egg albumen aids in a similar way the separation of bilirubin-calcium.

To a solution of bilirubin in ammonia, as nearly neutral as possible, a certain amount of calcium carbonate dissolved in carbonic acid can be added without any precipitate resulting, and none is formed even after standing for days, as long as the evaporation of carbonic acid is prevented. If, however, a little egg albumen be added to the solution, the whole of the bilirubin immediately separates out, and some calcium carbonate is likewise present in the precipitate.

Egg albumen brings about the separation of bilirubin-calcium from bile and from a solution of sodium glycocholate containing bilirubin, and in this case a large amount of calcium glycocholate is simultaneously precipitated.

It is highly probable that this property possessed by certain albuminous substances, of favouring the precipitation of bilirubin-calcium, plays an important part in the production of biliary concretions. We shall see later that it is principally the albuminous masses derived from the destruction of the epithelial covering of the mucous membrane that bring about the production of such precipitates.

CHAPTER IV.

The Formation of Gall-stones.

1. *History and Method of Investigation.*

Any one who is acquainted with the literature of gall-stone formation will understand my omission of any systematic epitome of it. One point only must be dealt with here.

It was the observations of nuclei in the centre of gall-stones which suggested to many the notion that the presence of such a nucleus is chief factor in the production of calculi, and that the presence of such a focus of crystallization suffices for the precipitation from the bile which stagnates in the gall bladder of materials, not easily soluble, from which the stones are formed, viz., cholesterin and bilirubin-calcium.

The possibility that this occurs cannot be questioned, but the majority of stones are formed in another way, as will be presently shown. Moreover, as can at any rate be readily shown in the case of dogs, the presence of a focus of crystallization does not suffice for the formation of calculi in bile. Some time ago, Labes, in my laboratory at Königsberg, introduced into the gall bladders of dogs various substances of irritating, infective, alkaline, and acid characters, which form precipitates with the mucus of bile, as well as actual gall-stones; and this last experiment I have recently repeated. No precipitation around the introduced body was ever obtained. At the final examination the foreign bodies when small or soft and yielding were no longer found in the gall bladder, having been expelled, whilst the larger and harder ones lay in the bladder more or less acted upon by the bile, but never incrusted. Introduced gall-stones, of whatever kind, were simply dissolved and ultimately disappeared.

For example, there were simultaneously introduced into the bile of a dog, without ligature of the duct: (1) A large crystalline piece of a cholesterin stone, weighing 0·365 grm. (after drying in the air). (2) A hollow cholesterin calculus (group 3) containing much bilirubin-calcium (weight 0·257 grm.). (3) A

similar stone, weighing 0·081 grm. (4) Small bilirubin-calcium calculi (group 4), weighing 0·048 grm.

The dog was killed two months later, when Nos. 3 and 4 had disappeared from the gall bladder, No. 2 dried in the air then weighed only 0·085 grm., and No. 1, similarly treated, 0·088 grm.

It is clear, then, that the presence of a focus of crystallization in no way suffices to cause the precipitation of the calculus-forming substances from a bile in which they are moderately abundantly present, and I may here add that in the human biles most richly impregnated with these substances I have never met with any appearance supporting the view that concretions are formed simply by such a crystallization out of the stone-forming substances around a focus of crystallization.

My investigations have been chiefly carried out upon the very abundant material afforded by my own collection of gall-stones, and especially by the Pathological Institute in this place.   By the kindness of Dr. v. Recklinghausen I have received during the past two years numerous gall bladders with their contents, for the most part unopened.

Transparent sections of the stones can be obtained in two different ways. On the one hand I have carefully extracted the stones with ether, and then embedded them in celloidin, as Posner had previously done, gradually replacing the ether in which the stone lay by celloidin solution. The stones thus embedded were then hardened and cut in the usual way. In this manner it is very easy to obtain quite thin sections of the smaller calculi, but the knife suffers considerably from the calcareous particles still present in the stones. I have made extensive use of ground sections, which are easily obtained of any thickness desired. If the stone as it stands is not hard enough to be ground, or if it contains cavities or fissures, it is first infiltrated with commercial isinglass and dried, and then cut across with the fret-saw and ground with a fine file.   The calculus is then fastened upon a microscope slide by means of isinglass, and the grinding is completed from the other side. I have myself made all my own sections in the dry with a broad file with as fine a grain as possible.   Objectionable file marks can be avoided by gentle filing, or one can in addition polish the surface of the section with leather slightly moistened with alcohol.

2. *The Mode of Origin of Gall-stones.*

(*a*) *The origin of gall bladder stones.* (*b*) *The origin of bili-rubin-calcium gravel from inspissated bile in the intrahepatic bile ducts.*

In the bile from the gall bladders of human corpses epithelium cast off from the mucous membrane is always present. Some-times separate cells float about in the bile, and sometimes they remain attached to each other in skin-like flakes. In the bile of young persons these are usually pale, and with the exception of their nuclei show nothing peculiar. In older individuals, and especially in those who have succumbed to tuberculosis, acute febrile disorders, or cardiac lesions, and always in cases in which formed calculi are present in the gall bladder, the epithelium is found to have undergone a fatty change.

Sometimes fat globules of various sizes are seen in the epithelial cells, especially in the neighbourhood of the nucleus, and sometimes they exhibit the well-known myeline appearances. In exceptional cases the cells are almost entirely filled with these doubly contoured myeline forms. One sees under the microscope how these myeline particles escape from the cells, and either float about singly in the bile, or even run together into larger lumps of a highly refractive, vitreous, structureless material.

Such masses of vitreous, structureless material are also occa-sionally found in abundance in the bile. They consist of nothing else than cholesterin, and one may sometimes see them solidify into a mass of cholesterin crystals when acetic acid is added to the preparation.

These cholesterin masses represent the ground-work of gall-stones. In addition to the still soft lumps of the kind just described, actual minute stones, of a harder consistence, but closely resembling them, are present. The material of which these are formed is at first completely vitreous, but sooner or later the cholesterin begins to assume a crystalline form.

Even from structures of this kind of 0·7 millimeter in diameter I have been able to prepare sections.

In cases in which the development of such minute stones from cholesterin particles could be observed, I have also regularly met with other minute cholesterin calculi of the smallest size, enclosing a central cavity filled with a brown

pultaceous material, consisting for the most part of bilirubin-calcium.

Moreover, the development of these very minute cholesterin calculi with centres of bilirubin-calcium can be followed from its very commencement.   One finds shreds of swollen epithelial cells which break down into granular brownish masses ; and in addition to such amorphous masses one sees others in which a complete differentiation into a vitreous (cholesterin) crust, consisting of confluent myeline forms, and a brown granular material which occupies the central portion, has taken place. All intermediate stages from such minute microscopic structures to small calculi, from which sections may be obtained, are just as well represented as in the already described development of pure vitreous cholesterin stones.

Perhaps a second mode of origin of the concretions is still commoner, that is to say an origin from the sedimentary masses which are frequently met with in human bile.   These are the flocculent, crumbly, brownish lumps which are seen under the microscope to consist of brownish particles and yellow gritty masses.   In them there are often abundantly present fat granules and even cholesterin crystals, as isolated tablets, or collected into groups.

On chemical analysis these masses yield fat, cholesterin, bilirubin-calcium, alkaline bile salts, and albuminous substances, mucus, &c. Their quantitative composition varies. They always contain much, and often very much, more cholesterin (in relation to their total solid constituents) than does the bile. In two analyses by Professor Minkowski the cholesterin content reached nearly 25 per cent of the solid residue.   Still more significant than their cholesterin content is the amount of the bilirubin-calcium which they contain.   In one case this amounted to as much as 33 per cent. of the solid residue.   The fats often reach 20 per cent., whilst the amount of alkaline bile salts is not infrequently 15—30 per cent. of the solid constituents, and even greater when there is little cholesterin and bilirubin. The bile acids are not combined with lime, but on the contrary, in the cases examined (Professor Minkowski's analyses), the amount of lime was just about a tenth of the bile pigment combined with alkalies, *i.e.*, just the calculated quantity required, if all the lime was combined with the bile pigment.   The

readily soluble alkali salts of the bile acids have no importance
in connection with the further stages of calculus formation, and
they rapidly disappear as the concretion hardens. Free bilirubin
(capable of extraction with chloroform) is never found in the
washed sediments in any but minute quantities, no greater than
can be ascribed to the bile with which they are still infiltrated.
Such masses are often found in the gall bladder welded together
into firm lumps attaining to the size of a cherry.   These lumps
are still very friable, but yet they can be transferred from one
vessel to another with careful management, washed, &c.   Such
masses have the same composition as the sediments described
above.

From the lumps here described gall-stones may be formed in
various ways.   One way in which they develope into calculi is
by becoming enveloped in a layer of bilirubin-calcium.   In
two different cases I have met with such beginnings of the
development of bile concretions in the human gall bladder.
Lumps of very various sizes almost completely filled up the
bladder, consisting of a yellowish somewhat soft material of
about the consistence of soft dough.

Under the microscope the mass showed in one instance the
appearance described above, whereas in the other there were
numerous microscopic clusters of radially disposed needles, or
small elongated tables (cholesterin).   The surfaces of the lumps
were clothed with a layer of brown bilirubin-calcium, and this
layer, although it was still very thin, so that it was easily
broken by any careless handling, was still firm enough to hold
together the entire structure.   They admitted of careful washing
with water and could be preserved unaltered for many weeks in
repeated changes of water.   On drying, the crust of bilirubin-
calcium was distinctly preserved, whilst the soft contents had
shrunk together into a very scanty coating on its inner surface.

In another and third case similar structures were observed in
a rather more advanced stage of development.   Here, indeed, one
had to do with actual gall-stones.   Unfortunately, they only came
into my hands long after they had been removed from the gall
bladder.   They had the appearance of six undamaged stones
varying from the size of a pea to that of a pigeon's egg, of
irregular form, and with smooth brownish-black surfaces.   One
was at once struck by their unusual lightness, and the surface

appeared flexible and broke on the slightest pressure. It was then seen that the concretions were completely hollow, consisting merely of a thin crust of bilirubin-calcium, about as thick and as hard as the shell of a sparrow's egg. In the cavity enclosed by this crust were a few fragments of a dry substance, in which cholesterin was found.

Whilst in this, or in another way, presently to be described, the freshly-formed structure has acquired its firm crust, the consolidation of the internal portion has also commenced. The first stage of this process consists in the separation of cholesterin and bilirubin-calcium in a firm mass from the amorphous detritus forming the nucleus. The cholesterin crystallizes out (the commencement of such crystalline separation of cholesterin in the pultaceous nuclear deposit has been already spoken of on p. 25), whilst the bilirubin-calcium consolidates into soft nodular masses.

It is easy to understand how the solid material of the nucleus, thus separating, becomes deposited upon the inner surface of the firm crust which has already been formed, which provides it with a *point d'appui*, whereas the fluid constituents collect in the central parts of the nucleus. This is the origin of the central cavity which is so often met with in immature concretions.

We have just seen how the pultaceous foundation becomes clothed with its first solid covering; but its consolidation may take place without the formation of such an independent crust. One finds in the gall bladder concretions which are still sufficiently soft to be easily crushed between the fingers like a lump of clay. These have already within them the cavity filled with liquid, the walls of which, as well as the substance of the stone, show no lamination. They consist rather of a crumbling substance, which has just the appearance of dried sediment of the kind already described. Under the microscope, too, the substance resembles such sediments, for it consists of granular or nodular deposits of bilirubin-calcium, with here and there crystalline cholesterin deposits, which appear under the microscope as clusters of tabular crystals. Such structures also are probably produced by the separation of the firm particles of the pultaceous deposit as an outer shell, and the collection of the fluid in the centre.

This may be due to the bile in which the pultaceous basis of the concretion is bathed becoming more concentrated owing to a long sojourn in the gall bladder. This must lead to a shrinkage of the basis which first affects its superficial layers. At the same time the mass dries from the surface inwards, and thus the earliest solid crust is formed, upon which the solid materials are deposited when they begin to separate out from the original pultaceous mass. It is obvious that whether or no concretions are formed from the pultaceous material depends upon a variety of circumstances which may be called accidental.

If an evacuation of the gall bladder takes place before the soft material has had time to solidify, it passes out innocuously; but if its stay in the gall bladder is longer, it acquires a firmer consistence, and it may then remain behind in the gall bladder when the liquid bile is evacuated; after that the further consolidation can be rapidly completed, since by compression by the walls of the gall bladder the fluid is expressed from the viscious mass.

These soft masses are often flask-shaped, and are bent and doubled up by the contractions of the gall bladder. This is the best explanation of the irregular forms which small freshly-formed stones so often exhibit.

Whilst still soft the masses may adhere together, and thus are formed the raspberry calculi. Such recently-formed stones usually contain the central cavity filled with liquid which has been already described; and this is, in spite of the numerous nodular processes and excrescences, usually common to the whole mass, which affords a proof that the separation into the firm crust and the cavity filled with fluid has only taken place after the concretions had become welded together in a soft state.

In quite exceptional cases I have met with quite another mode of formation of calculi in the gall bladder. I have occasionally found in the gall bladder small nodular masses of apparently pure bilirubin-calcium which have obviously adhered together to form small concretions. In only one single instance have I seen the production of concretions by the adhesion to each other of tabular crystals of cholesterin. The bile contained such crystals in large quantities, and it was easy to convince oneself that they were rolled together and welded into solid lumps. Amor-

phous precipitates of bilirubin- and biliverdin-calcium appeared
to serve as a cement substance.

(c) *The formation of bilirubin-calcium gravel in the bile ducts
within the liver.*—These small calculi have been already suffi-
ciently described (I., No. 5), and it has been already stated
that they are frequently formed in the ducts within the liver.
One finds one or other of the larger bile ducts filled with
thick, greasy, brownish-black bile, in which are enclosed the
calculi, varying from the very finest gravel to nodular and stalked
masses.   At first one might easily get the impression that these
structures are simply produced by the inspissation of bile, but
their formation is certainly not so simple, since they consist of
calcium compounds of the bile pigments, and precipitates of
these substances are not produced by mere concentration of
the bile.   Moreover, they are markedly differentiated from
inspissated bile in that they contain large amounts of the
higher oxidation products of bile pigment and bilihumin.

The constant presence of bilihumin in such concretions has suggested
to me whether it is not the case that humous substances derived
from the food are excreted with the bile and precipitated in the biliary
passages. I have made experiments upon this point with a large
·number of substances which yield or might yield humous substances in
the body, but such humous substances never passed over into the bile.

Moreover, one finds in such concretions—in biliverdin, bilicyaniu,
and bilifuscin—the transition substances between bilirubin and humin,
and consequently one must certainly conclude that this last originates
in situ from bile pigment.

At any rate, then, there are at work in the formation of
concretions in this situation oxidation processes which do not
usually take part in so energetic a manner in the formation of
concretions in the gall bladder.*

In explanation of this it should be pointed out that the
concentrated bile in the ducts is subjected in a high degree
to the influence of the living tissue of the mucous membrane.
Very likely, too, scizomycetes, which readily grow in bile when
it is stagnant, give rise to the oxidation.

* There often exists, in cases in which these stones are met with in the intra-
hepatic ducts, general biliary obstruction in the liver, as, for example, with new
growths, cirrhosis, obstructive congestion. As is well known, one often finds in
such conditions nodular masses of bile pigment deposited in the capillary intra-
lobular ducts, but I have not been able to establish any connection between the
formation of gravel and such deposits.

3. *The Further Development of Concretions.*

In the further development of the earliest bases above described into fully-formed calculi two different processes go hand in hand. The first of these is the growth of the stones, which is chiefly due to the addition of fresh layers. Secondly, very extensive transformation takes place in the concretions, which takes the form, in most cases, of a continuously progressive infiltration with cholesterin and the deposit within the concretions of this substance in crystalline form.

(*a*) *The growth of stones by deposition from without.*—The growth of stones is mostly due to the addition of concentric laminæ. These laminæ consist either of almost pure white cholesterin or they contain admixtures in varying amounts of bilirubin-calcium or more rarely biliverdin-calcium. The former are white; the latter yellow to brown or green.

In this way a thick crust, which is often quite hard, is formed, whereas the nucleus is still soft and the central cavity remains filled with liquid. The individual laminæ are for the most part narrow, hardly more than a millimeter in thickness, or even much thinner; but this is only true of the white layers consisting of more or less pure cholesterin. The layers which are rich in bilirubin-calcium are often of considerable thickness, reaching five or more millimeters. Layers of bilirubin-calcium can, of course, only be deposited when bile can enter the gall bladder. On the other hand, a further growth of a calculus by deposition of cholesterin may take place, when the calculus is incarcerated in a gall bladder with closed cystic duct, or is embraced by the mucous membrane in a diverticulum of the gall bladder; and when all access of bile to it has long been rendered impossible the mucous membrane itself still furnishes cholesterin. I have often removed calculi from such situations, which have exhibited upon their surface a pultaceous layer of cholesterin in myeline forms or in small crystals, without any admixture of bilirubin-calcium. Where layers of pure cholesterin alternate with brown layers of bilirubin-calcium the former are possibly deposited in the gall bladder when it is empty, the latter when it is filled with bile. Such an alternation of conditions must be the rule, since when gall-stones are present the cystic duct is, as a matter of fact, often enough temporarily blocked.

(b) *The development of the crystalline structure of calculi by the crystallizing out of cholesterin, and cholesterin infiltration.*— Pure and laminated cholesterin calculi constitute the majority of the larger gall-stones. They usually show a very distinct crystalline structure. Naturally such crystalline cholesterin stones have always specially attracted the notice of observers. Their definitely crystalline structure seems to show that gall-stones originate and increase by crystallization from solution, and yet such calculi are one and all secondary formations. Only Meckel v. Hemsbach has correctly grasped this fact, but the numerous accurate statements of Meckel on this point are only given very briefly in his "Microgeologie," which was published after his death by Billroth. They have consequently not received the amount of attention which they deserve.

With a view to studying the transformation which these concretions undergo in the course of their further development I have prepared sections of such calculi by the method described above, which were thin enough to be examined by transmitted light, and have had photographs of such sections prepared, which were enlarged to five or ten diameters. Such photographs of sections allow the structure of the stones to be very clearly seen. On examining these it is at once perceived that the crystalline structure of such stones is due to a secondary crystallization of cholesterin taking place within the calculus. It seems to me impossible to interpret the appearances in any other way.

Moreover, I have not omitted to seek the opinion of a competent mineralogist, my colleague, Herr Bücking, of this place. His opinion is as follows:—" There is no doubt that one is here dealing with a crystallization of cholesterin in calculi which have already become consolidated, and, moreover, this crystallization has proceeded from the centre towards the periphery of the stone."

Such subsequent crystallization of cholesterin may be either of the nature of a crystallization of already included cholesterin, or of the formation of crystals from cholesterin which has made its way into the calculus. No doubt both processes have a share in producing the result, but it is quite certain that a crystallizing out of subsequently introduced cholesterin takes place, *i.e.*, a secondary infiltration of the calculus with choles-

terin. Herr Bücking was good enough to call my attention to the significance in this connection of the channels of infiltration so familiar to mineralogists. These are canals which penetrate the crusts of the concretions, and by which soft masses of cholesterin derived from the epithelium, or from the bile containing this substance, are able to effect an entry. They are to be found in many sections, and several frequently occur in the same section. The already fully hardened calculi completely infiltrated with cholesterin present themselves under two distinct forms :—

(a) Some still present no such coarsely crystalline structure as can be recognised with the naked eye, but show a nucleus which is clearly differentiated from the laminated crust. The layers of the crust consist of vitreous cholesterin (in some cases mixed with a greater or less amount of bilirubin-calcium). The nucleus is formed of closely-compressed clusters and stalactite-like masses of cholesterin, which, under the microscope, exhibit a finely crystalline radiating striation. As was mentioned on p. 26, microscopic clusters of cholesterin crystals are often met with in the first stages of the calculi, whilst these are still quite soft, and it is probably by the growth of these that the solidification of the nucleus is brought about in such specimens.

(b) Calculi of the second class, viz., with coarsely crystalline structure, frequently no longer show a nucleus which is clearly marked off from the crust, and often, too, the laminæ are no longer distinct.

Stones are, however, frequently met with which possess a nucleus which has a distinct border towards the cortex, which nucleus exhibits, as a rule, a stalactitic structure, such as was described under (a), but in its centre distinct crystals are clearly visible.

The earliest and largest crystals are always formed in the central portions of the nucleus. The fact that they first appear in this situation is very likely due to the fact that the calculi had a central cavity in which the cholesterin, which penetrates into them from without, can be deposited in well-developed crystals.

From such crystals deposited in the centre the further development of the crystalline structure proceeds. When crystals are once formed they are able to grow by assimilating

to themselves the neighbouring cholesterin masses, even when these have been themselves deposited in a solid and even in a crystalline form.   Such phenomena are well known to mineralogists.   Moreover, the cholesterin, which is brought to them through the channels of infiltration, is also capable of being utilized for their growth.

By the continuous growth of the original crystals, and the addition of other crystals to them, the cholesterin gains more and more ground.   The crust becomes involved in this crystallizing process, which gradually gains the mastery.   The other constituent of the calculus (bilirubin-calcium) is displaced, and disappears.   It perhaps passes into solution (for there is no doubt that bilirubin-calcium is soluble in bile), or perhaps mechanical influences come into action.   Such processes are often called into play in the formation of crystals, but they have not yet been explained by mineralogists.   In this way the well-known pure cholesterin stones are formed, the " *cholesterin-solitäre*," as Meckel first called them.

CHAPTER V.

1. On the Production of the Calculus-forming Substances and the Manner in which they are made use of in the Construction of Gall-stones.

2. On the Origin and Growth of Concretions which contain Cholesterin, outside the Gall Bladder.

In Chapter II. it was shown that the cholesterin and lime of normal bile are probably derived from the mucous membrane of the biliary passages.* We have further seen, in Chapter III., that the cholesterin which is made use of in the formation of calculi has, for the most part, never been in solution in the bile. The origin of the amorphous sedimentary masses which form the commonest material for the construction of concretions is less clear. It would appear that these also sometimes originate in disintegration of epithelium. One frequently finds collections of epithelial cells in which the myeline forms of cholesterin, and bilirubin crystals are to be seen in quantities, and I have convinced myself that the amorphous masses are produced by the disintegration of such cells. In these bilirubin exists as bilirubin-calcium, and it seems as if in the disintegration of the cells bilirubin-calcium is formed from bilirubin. Yet such observations are by no means conclusive, for usually no such production of sedimentary masses can be demonstrated, and lastly there can be no question that precipitation of bilirubin-calcium can take place from the bile itself. The following observations render it probable that occasionally this actually happens :—

Not unfrequently brown bilirubin-calcium stones are met with of the size of a pigeon's egg, or even larger, the shape of which clearly shows them to be casts of the gall bladder. They

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* Shortly before this work was completed I found that Bristowe has already suggested (in 1887) that the cholesterin of which calculi are formed is secreted by the mucous membrane of the gall bladder. He bases his opinion on a case in which he found the gall bladder almost completely obliterated. In certain spots there were small cavities enclosed by mucous membrane, and in these were lumps of soft cholesterin.

fall to pieces on drying, and a nucleus is found, which may be of any nature, enclosed in a thick coating of bilirubin-calcium, a centimeter in thickness. This coating shows no lamination, and has to all appearance been precipitated all at once from the bile, the whole of the bile contained in the gall bladder having solidified into a precipitate of bilirubin-calcium. It may be that the cause of the origin of this precipitation in bulk may have to be sought in a peculiarly rich secretion, or the formation from a diseased mucous membrane of a secretion peculiarly rich in lime; and the morbid disintegration of epithelial cells may favour the precipitation of bilirubin-calcium in so far that the products of disintegration contain albumen, and the presence of albumen in solution favours the separation of bilirubin-calcium.

The calculus derives the cholesterin required for its future growth and for cholesterin infiltration from two sources. In the first place the disintegrating epithelium of the bile passages may yield this material. There can be no doubt that this occurs in cases in which one finds the stone enclosed in a layer of pultaceous cholesterin, or when it is removed from an obliterated gall bladder, or from a pocket in which for a long time no bile has been able to enter, and in which it lies embraced by the mucous membrane. The material penetrates the stone by way of the infiltration channels, which in this way may grow by deposition of cholesterin and by infiltration therewith, without any longer coming into actual contact with bile. Where, on the other hand, the stone is bathed in bile, it can grow in a second way, by crystallization of cholesterin upon it from the bile. Many calculi show obvious indications of this. These are always pure cholesterin calculi, almost always of about the same size (that of an almond), which float at large in the gall bladder, and on the surfaces of which the edges and facets of cholesterin crystals are clearly seen. This is the appearance presented by nuclei which grow by the deposition of crystals upon their surfaces.

However I would emphasize, once for all, the fact that we seldom meet with specimens which afford proof of such increase by the deposition of crystals of cholesterin from the bile, and further that even such stones are not originally formed by the crystallization out of cholesterin from the bile. On the other hand sections have shown in all cases in which I have investi-

gated the point, that structure, which affords evidence of their
formation by secondary crystallization of cholesterin.

In the great majority of calculi, even of the pure cholesterin
variety, the complete absence of any superficial crystalline
structure shows that their growth has not been brought about
by the deposition in crystals of the cholesterin which is dissolved
in the bile. I have only in a single case seen a true produc-
tion of concretions from free crystals separated in the bile.
(Conf. p. 26.)

2. The formation of small bilirubin-calcium calculi in the
small intra-hepatic ducts has already been frequently alluded
to. With this exception, the origination of concretions appears
to be confined as a rule to the gall bladder. This is easy to
understand, seeing that their earliest (soft) beginnings can
hardly remain in the larger ducts, as long as these are
patent.

Under exceptional circumstances calculi can even originate
in the large bile ducts, and it frequently happens that stones
from the gall bladder make their way into the large ducts and
there remain fixed. There they increase further in size ; their
growth being here due, as in the gall bladder, to bilirubin-
calcium and cholesterin, and they develop in the ducts, just as
in the gall bladder, into mixed bilirubin-calcium or pure choles-
terin stones.

There are to be found, as has been already mentioned, in the
large bile ducts, as in the gall bladder, calculi of cholesterin,
tightly enclosed by the mucous membrane of the duct. These
are far too large to have been carried to the positions in
which they lie, and appear to have grown upon the spot,
and to have undergone cholesterin infiltration, although the
bile has for a long time had no access to them. Since the
cholesterin has its origin in the epithelium of the biliary
passages, there is no ground for supposing that this material for
the formation of stones may not be just as well yielded by the
mucous membrane of the ducts as by that of the gall bladder
itself, since both possess (according to Ranvier) an exactly
similar epithelium. Both possess, in addition to cylindrical
cells, repairing cells, so that the disintegrated epithelium can
undergo regeneration, and can produce cholesterin by repeated
disintegrations. In the smaller bile ducts these repairing cells

are wanting, and with them probably the possibility of the production of cholesterin in any considerable quantities.

Except in the bile passages the formation of concretions which contain much cholesterin is a very uncommon event. I can only adduce a single example; that of bronchial calculi, the analysis of which by Sgarzi (which I find recorded by Robin) gave 20 per cent. of cholesterin. The fact that cholesterin stones are so seldom formed elsewhere than in the gall bladder does not imply that no cholesterin production goes on elsewhere. Soft accumulations of cholesterin are found in numerous situations, such as atheromatous cysts, in cysts of the pancreatic ducts, &c., but here the cementing substance is wanting, whereas in the bile, bilirubin-calcium supplies a material specially suited for this purpose. Moreover, the gall bladder offers a place of refuge in which the newly-formed concretions can undergo further development undisturbed, and their consolidation may be favoured, as has been mentioned on p. 28, by the compression exerted by its muscular coat.

CHAPTER VI.

The Causes of Cholelithiasis.

The results dealt with in the preceding sections agree in pointing to the conclusion that the formation of concretions in the bile is dependent upon a morbid process in the mucous membrane of the biliary passages. At any rate they afford no indication that the influences of food or of metabolism come into play as causes of gall-stone formation.

1. General Ætiology of Cholelithiasis.

a. *Statistics and the conclusions to be drawn from them.*

Accurate statistics of the occurrence of gall-stones can only be based upon *post-mortem* data. The diagnosis of cholelithiasis during life is far too uncertain, as is very clearly shown by the fact that it is actually in old people in whom these concretions are commonest that they are least frequently diagnosed.

Numerous statistics showing the frequency of biliary calculi post-mortem have been already published, as for example by Fiedler for Dresden, by Peters for Kiel, two sets by Roth for Basle, by Rother for Munich, by Frank for Vienna, and by Schloth for Erlangen. Schröder also has recently, at my instigation, availed himself of the post-mortem data of the Pathological Institute in Strasburg for the construction of a table of this kind. According to—

Peters (Kiel)	gall-stones were found in		$5\,°/_o$ of the bodies examined.		
Rother (Munich)	,,	,,	$6\,°/_o$	,,	,,
Fiedler (Dresden)	,,	,,	$7\,°/_o$	,,	,,
Schloth (Erlangen)	,,	,,	$7·2\,°/_o$	,,	,,
Roth (Basle) I.	,,	,,	$9\,°/_o$	,,	,,
,, ,, II.	,,	,,	$10·9\,°/_o$	,,	,,
Frank (Vienna)	,,	,,	$10\,°/_o$	,,	,,
Schröder (Strasburg)	,,	,,	$12\,°/_o$	,,	,,

It might appear from this that gall-stones occur with very different frequency at different places, but such results are liable to several kinds of error. To one of these Fiedler has

already called attention, viz., that gall-stones are easily over-
looked at post-mortem examination, and that as a consequence
the frequency of their occurrence is often stated too low.

This source of error is all the more misleading, because its
amount can obviously not be estimated and is very variable.
Again the results from the various pathological institutions are
not strictly comparable, because the various periods of life are
not equally represented in the material. The frequency with
which gall-stones are found must prove considerably less, where
a relatively large proportion of young persons, under 30 years,
and much greater where many old people come under examina-
tion, since, as has been already mentioned, such concretions are
found in 2—3 per cent. of the members of the first class, as
against 25 per cent. of those of the latter.

Schröder, in Strasburg, has made use of the material from
the great Strasburg Hospital, placed at his disposal by Professor
von Recklinghausen, and his statistics are based exclusively
upon the autopsies carried out by Professor von Recklinghausen
in Strasburg during the years 1880-1887. Herr von Reckling-
hausen vouched for the fact that gall-stones had not been
overlooked in any of these cases. Schröder's material had,
moreover, the advantage of including all periods of life, since
the Strasburg Hospital includes both a children's and an
infirmary department, the latter of which yields many post-
mortems.

In the discussion which follows, I shall take my stand chiefly
upon Schröder's statistics, and I can do so the more readily
because in the essential particulars the results show no impor-
tant differences from those of the earlier collections.

As regards the frequency of gall-stones in persons of different
ages, information is furnished by the following table of
Schröder's :—

TABLE VII.

Age of patients.		Number of post-mortems.		Number of cases with gall-stones.		Percentage of cases examined, in which gall-stones were present.
0—20	...	82	...	2	...	2·4
21—30	...	188	...	6	...	3·2
31—40	...	209	...	24	...	11·5
41—50	...	252	...	28	...	11·1
51—60	...	161	...	16	...	9·9
60 and over	...	258	...	65	...	25·2

Schröder further found the presence of gall-stones noted :—

Among males, in 4·4 per cent. of the bodies examined.

Among women, in 20·6 per cent. of the bodies examined.

Among 115 adult women there were 99 who had certainly borne children, only eleven had certainly not borne children, and in five instances this point could not be definitely decided. Leaving these five aside, it appears that of the women who had died during the child-bearing period or later, and who were afflicted with gall-stones, only 10 per cent. has never passed through pregnancy.

The statistics teach then :—

1. That gall-stones are uncommon in young people under 30 years, commoner after 30, and very much commoner in old people over 60 years of age.

2. That they are much commoner in women than in men.

3. That among women they are much more frequent in those who have borne children.

The conclusion which must be drawn from these facts, and which is also based upon general considerations, is that the formation of gall-stones is immensely favoured by any condition which interferes with or retards the flow of bile.

We can easily understand that this is the cause of the excessive frequency of gall-stones in females, since their style of dress and pregnancy are both calculated to bring about disturbances of the flow of the bile. The liver of tight lacing, which is so common in females, is the recognized indication of the violence which this organ so often undergoes as a result of the unsuitable dress of our women. Marchand, Riedel and Rother long ago showed that this lesion is very commonly associated with cholelithiasis. Schröder found gall-stones in more than half the females on whose liver the groove in question could be recognised.

Pregnancy, and the pendulous abdomen which is apt to follow it, often leads to a loosening of the abdominal viscera from their places, and favours the production of floating liver or kidneys.

Both these causes then, the deformity of liver by tight lacing and the disturbance of the normal situation of the organs, specially affect the gall bladder. Riedel has shown that the gall bladder is usually turned downwards with the compressed

lobe, whereby the cystic duct is stretched and the emptying of the gall bladder rendered more difficult.

Weisker has moreover very clearly demonstrated that in cases of floating liver or right kidney a stretching of the *ligamentum hepatico-duodenale* is produced, which again specially affects the cystic duct and thereby hinders the evacuation of the gall bladder; and previous to him Litten had already pointed out that movable kidneys are capable of causing biliary obstruction.

But even apart from any such coarse lesions, the bile stream is liable to be hindered by the dress of women, and in pregnancy. We know that the expulsion of the bile from the common duct is materially aided by the pressure to which the liver is subjected by the movements of the diaphragm in respiration; this has been proved by the experiments of Heidenhain and his pupils. In women the stays keep the diaphragm at rest, and in pregnancy the same result is produced, but in a different way. The absence of diaphragmatic respiration and the exclusively costal type of breathing in women is not favourable to the flow of bile.

It is less easy to understand the reason of the fact that the frequency of gall-stones increases so conspicuously with advancing years. It is true that gall-stones occur even in earliest childhood, and Lieutaud and Porbal have in exceptional cases found them in new-born infants.*

Frerichs has met with them in a child of five, yet they only become more common in the third decennium and excessively common in old age. It might be supposed that in old age the excretion of cholesterin is increased—(Table VIII., p. 42, gives, after Kausch, an epitome of cases, at very different ages, in which death was due to various diseases, and in which gall-stones were absent: they certainly show the presence of larger amounts of cholesterin in the bile of the elder individuals)—and it is not improbable that advancing age favours the disintegration of the epithelium of the mucous membrane with the formation of cholesterin, just as it favours the atheromatous process in the arterial walls, in which also cholesterin is produced.†

* Valleix states that concretions are somewhat frequently to be found in the gall bladders of new-born infants. The frequently quoted cases of Cruveilheir's does not belong to this category.

† Becquerel and Rodier found the blood of old people richer in cholesterin than that of the young.

Probably, however, interference with the flow of bile here again comes into play. The bile passages are endowed with unstriped muscle fibres, and it is certain that contractions of their walls play a part in the expulsion of the bile, so that we may well accept atony of the bile ducts as a cause of retarded expulsion of bile in old people, just as the tardy expulsion of the fæces and urine in such persons is quite commonly ascribed to atony of the intestine and bladder. Charcot actually found that the unstriped muscle-fibres in the walls of the biliary passages underwent very extensive atrophy in old people, and thus the cause of the atony of old age was clearly demonstrated. Moreover, we must suppose that in the aged the mucous membrane of the bile passages suffers a loss of resisting power, as all their other tissues do.

TABLE VIII.

	Post-mortem Diagnosis.	Age.	Percentage of cholesterin in solid constituents of the bile.
1	Mitral stenosis	27	... 2·64
2	Phthisis pulmonalis, Erysipelas ...	28	... 1·97
3	Nephritis	34	... 1·30
4	Peritonitis	37	... 1·35
5	General eczema...	42	... 1·95
6	Pneumonia after amputation of thigh	45	... 1·57
7	Cirrhosis hepatis	45	... 2·9
8	Carcinoma of rectum	49	... 2·12
9	Rupture of intestine	50	... 1·12
10	Carcinoma of superior maxilla ...	56	... 2·8
11	Fracture of cervical spine	66	... 3·86
12	Pneumonia	68	... 2·96
13	Pulmonary embolism	77	... 2·36

Moreover, the more frequent occurrence of gall-stones in the bodies of the aged does not prove that the calculi are *formed* so much more frequently in old than in young people. It is quite possible that they are produced with about equal frequency at all ages, and that they are only found so much more commonly in old persons because with them there has been more time to allow of their formation.

Two further points should be here referred to. First :—The more frequent occurrence of cholelithiasis in persons who lead sedentary lives.—After what has just been said it is easy to understand that active bodily movements aid the flow of bile,

and so hinder the formation of concretions. Secondly:—
Frerichs has attributed a share in their production to infrequent
meals and the associated too infrequent evacuation of the gall
bladder. This is *a priori* obvious, but facts bearing upon the
importance of this cause are wanting.

(B) *Heredity, Diatheses, Constitutional Anomalies, Peculiarities of Diet, as presumed causes of Cholelithiasis.*

Numerous authors give examples of the occurrence of chole-
lithiasis in nearly related members of the same family, as for
example, Roth, Kraus, and others. Yet such examples do not
appear to be common, and, in the case of a disease which is so
widely distributed, it does not serve as a proof of heredity even
that several members of a family suffer from it.

Again the view has frequently been propounded that the
development of cholelithiasis is favoured by certain diatheses
and constitutional anomalies, as well as by pecularities of diet.
For example, the more frequent occurrence of the disease in the
gouty and in those who suffer from atheromatous degeneration
has been asserted.

The unduly frequent occurrence of gall-stones in association
with atheromatous degeneration has been asserted by Benecke,
but this assertion does not appear to be well-founded, seeing
that in the statistics of Schloth (Erlangen) and also in those of
Schröder (Strasburg) atheroma was noted in 25 per cent. of the
cases with gall-stones. This is by no means an excessive propor-
tion, since at least 75 per cent. of the bodies in which gall-stones
were found were those of persons over 40 years of age. The
idea that gall-stones are unusually frequent in the gouty is
based, as far as I have been able to make out, merely upon the
impression which a few medical men have acquired in practice.
There is no firmer foundation for the views that obesity, and
slowness of metabolism, luxurious modes of life, and alcoholism
favour the production of the concretions. Nothing of the kind
has been proved, or even rendered probable, and the opinions
of authors upon these points stand in glaring contradiction to
each other. Whereas some (for example, Kraus) hold luxurious
modes of life responsible, other reliable authors (Albers) think
that gall-stones are commoner in "poor and ill-nourished
persons."

The impression which I have formed from my own experience, and from the study of the literature of the subject, is that we are here dealing with unfounded opinions, and that gall-stones apparently occur with equal frequency in people of all constitutions and degrees of nutrition.

Among the numerous time-honoured views upon the causation of cholelithiasis there is still one which must here be referred to. It is believed that in certain parts of the world gall-stones are much commoner than in others, and this has been associated with the influence of diet; yet it has seemed to me, the longer I have studied the subject, more and more questionable whether there is any sufficient grounds for believing in this excessive frequency of gall-stones in certain places, which has been generally accepted.

It may be, no doubt, that statistics appear to show that calculi occur with very varying frequency in different places, but the objections which render them inconclusive have been already stated. This much at any rate they seem to me to show, viz., that amongst populations which live under very different conditions as to the climate, nature of soil, and diet, such as those of Dresden, Vienna, and Basle, cholelithiasis occurs with nearly equal frequency.

Nearly related to the view under consideration is another, viz., that the frequency of gall-stones in certain regions is dependent upon the amount of calcium salts present in the drinking water. This last assertion, that the hardness of drinking water is the cause of the frequency of cholelithiasis in the places concerned, is not proved to be a fact. Yet it finds still so many adherents that it is necessary to demonstrate how devoid it is of any foundation. First of all the fact must be once again emphasized that, in dogs at any rate, the amount of calcium compounds in the bile undergoes no increase whatever when food rich in lime is administered. This speaks decidedly against the above view, but its supporters might reply as follows :—The lime salts of the bile are possibly derived from various sources. It is possible that food rich in lime salts leads to an increase of such salts in the secretion of the mucous membrane, which increase is nevertheless not shown in the total lime-contents of the bile, because the lime derived from this source constitutes too small a part of this total. Yet this increase

of the lime salts of the mucous secretion might be the actual determining cause of the formation of gall-stones, by leading to the formation of precipitates of bilirubin-calcium upon the surface of the mucous membrane, *i.e.*, at the point where the lime-containing secretion mixes with the bile. Naturally this question cannot be settled, as far as the mucous membrane of the gall bladder is concerned, but as regards the intestinal mucous membrane it has been decided by a still unpublished research of Socin of Basle, who has found that in dogs the amount of calcium salts in the mucous membrane of the intestines is practically the same, whether the diet be very rich or poor in lime salts. At present, then, we have no right to assume that the amount of lime salts in the secretion of the mucous membrane of the gall bladder is to any greater extent dependent upon diet.

It is only in order that nothing may be omitted which has possible bearings upon the subject that I allude to a further influence of diet upon the constitution of the bile, which may possibly play a part in the causation of cholelithiasis, viz., its effect upon the amount of bilirubin in the bile, which appears to be not without influence in the production of sediments of bilirubin-calcium. In bile rich in bilirubin, bilirubin-calcium appears to be more quickly deposited on the addition of lime, and, moreover, the amount of bilirubin in the bile appears to be dependent upon the food, being apparently much more abundant with a good than with a scanty diet.

However, stagnation of the bile remains the only well-established cause of the formation of gall-stones. After all that has been said in the previous sections, it is hardly necessary to insist once more that concentration of the bile, as such, does not lead to calculus formation. The fact requires to be firmly grasped that the excessive production of the constituents of the calculi, and the consequent formation of the calculi themselves, presupposes a morbid change in the epithelium of the mucous membrane.

The next question is : How can stagnation of the bile in the biliary passages give rise to the morbid process in their mucous membrane, which leads to the formation of calculi ? It seems to me that two possible explanations are sufficiently well-

grounded to call for mention, viz., that the bile exercises a deleterious action upon the epithelial covering of the mucous membrane, which action is increased by the slowing of its flow; or that the slowing of the stream in the biliary passages facilitates the introduction into them of ferments present in the duodenum, and that among these ferments are some which are capable of producing disease of the mucous membrane.

I will begin by discussing the second hypothesis.

In its support the following points may be adduced:— Normal bile is sterile. Netter has established this for rabbits by modern culture methods, and I can confirm the statement as the result of experiment on dogs and rabbits. In human beings also the bile in the normal condition appears to be sterile; Gilbert and Girode found it so in six out of eight cases, even 24 hours after death, and, moreover, in two cases, in which death was due to phthisis-pulmonalis, I also found the bile (taken from the body one and five hours after death) sterile, and the same in two cases of puncture of the distended gall bladder during life, for carcinoma and simple (paralytic) distension.

In association with stagnation of bile, micro-organisms frequently occur in that secretion. The first definite statements on this point were by Charcot and Gombault. They frequently found in dogs, after ligature of the common duct, bacilli and spores, which often formed mobile chains. I can confirm the occurrence of bacteria in the bile of the gall bladder, which has thus become concentrated. Netter found constantly (in 1886) that within as short an interval as 24 hours after aseptic ligature of the common duct in rabbits (close to the duodenum) cultures of bacteria could be obtained from the bile. In addition to staphylococci he found a bacillus. This same bacillus apparently —which is, it may here be stated, the *bacterium coli commune*— has now been detected in the bile passages, together with staphylococci and streptococci (which Netter and Martha, Brieger, Leyden, and others found in the human biliary passages in suppurative conditions, but usually alone) in a large number of cases. Gilbert and Girode found it in two cases in the normal bile passages 24 hours after death. In cholangitis it has been cultivated from the contents of the biliary passages by Netter and Martha, by Gilbert and Girode, and by Bouchard. In a case from my wards with hepatic abscess, due to gall-stones,

Levy obtained from pus of the abscess the *bacterium coli commune* in pure cultures ; and I have myself obtained this bacillus from the gall bladder by puncture during life in five cases of chole-lithiasis. In all these cases there was an acute, and in some cases an extremely acute, cholecystitis, probably developing in the course of a few days, and associated with unquestionable biliary colic.

The first case, which I will relate in full, was that of a young and well-developed girl, who had developed the gall bladder tumour 3 months previously in connection with acute colic. An exploratory puncture yielded a fluid almost as clear as water but rendered slightly turbid by pus. Three gelatine plates were moistened with this fluid, and upon each of these grew numerous colonies of the same organism, and by inoculation from the different colonies the same bacillus was always obtained. Examination of hanging-drop and unstained preparations showed short thick rods, usually arranged as diplo-baccilli, rarely in groups of four to six individuals. The bacillus showed a resemblance to that of Escherich (*bacterium coli commune*) and also to Friedlander's *diplococcus pneumoniæ*. Its length was 1·2—1·25 μ and it was somewhat actively mobile.

On gelatine plates : 1. Superficial colonies, after 8 days, 3 mm. in diameter; grey, thin pellicles with slightly notched edges. 2. Deep colonies, much smaller, brownish, circular or oval, with sharp contours. Gelatine stab-culture, a grey streak in which the individual colonies are recognized with difficulty as small granules. Glycerin-agar stab-culture at 37°C., abundant surface growth, after a short time a grey pellicle, covering the entire surface. Turbidity of the condensation water.

Bouillon-culture : uniform turbidity, clearing incompletely after 3 days, with flocculent sediment ; no capsule formed. In sterile human bile, from a fistula, the organism grew as in bouillon.

Potato-culture : fairly thick, dirty grey, crusts.

The bacillus grows well in all media at the temperature of a room, extraordinarily rapidly at 37° C., also grows anærobically ; does not liquify gelatine ; is stained by Gram's method.

Mice died after 12—24 hours, and the bacilli were present in moderate numbers in the blood and enlarged spleen. A pure culture was injected into the gall bladder of two dogs, after

the common duct had been tied. The first dog died of peritonitis 36 hours later, the second died 74 hours later. In the peritoneal exudation, contents of the gall bladders, and blood from the hearts of both dogs, this bacillus alone was found. (Confirmed by cultures.)

In both cases there was severe cholangitis, with moderate growths of bacilli in the bile. These frequently exhibited slight bulbous swellings at their ends (spores?) and the appearance of short threads. In both dogs the liver was much swollen, hyperæmic, and in that of the dog which died after 74 hours there were numerous necrotic foci.

As has been said, the bacillus closely resembled that of Escherich (*bacterium coli commune*), and only differed from it in being pathogenic for mice, and in growing upon potato in grey instead of in yellowish brown crusts. Bouchard obtained similar results with the bacillus which he cultivated.*

In the second case also I found a bacillus which agreed in all respects with that just described, except that it grew upon potato in yellow crusts. In the third case the same bacillus was found; but it formed grey crusts on potato, which turned brown later. In this instance the pathogenic properties of the bacillus for different species of animals was thoroughly investigated by Dr. Weintraud, whose report is appended.

Z., 69 years of age, female. Cholelithiasis; empyema of gall bladder; admitted October 6th, 1891, died October 15th, 1891.

On October 8th, 1891: Exploratory puncture of the gall bladder; a syringe full of (sero-purulent whitish, not yellowish) fluid removed. Under the microscope: abundant detritus-granules, numerous pus-corpuscles, a few granular masses, a few polygonal cells with large rounded nuclei, lying in contact like epithelial cells (liver cells?). An agar and a bouillon tube were impregnated with the fluid. From the bouillon tube two agar plates were moistened, and several agar tubes were directly inoculated.

On October 9th, 1891: Numerous colonies on both agar plates;

* In explanation of the hesitation manifested in identifying the bacillus here met with with the *bacillus coli communis*, it should be pointed out that at the (time 1891) this bacillus was not regarded as a pathogenic organism. The observations here recorded were, as far as I know, the first which demonstrated its pathogenic properties.

1, superficial, larger, whitish, with translucent edges; 2, deep oval and rounded, of a rather yellower tint. By inoculation from them, it was found that both were colonies of the same bacillus, which also, by direct inoculation on to agar tubes, grew in pure cultures. The organism was a small, slowly mobile diplo-bacillus, readily stained by Gram's method, or with methylene blue, growing upon gelatine in white moist colonies, which ran together into drops with a fatty lustre—non-liquefying.

It grew upon potato in a white layer, which later became distinctly brown.

October 10*th*, 1891 : A mouse was inoculated in the peritoneal cavity with one drop of the condensation water from an agar culture one day old.

October 11*th*, 1891 : This morning the mouse died. Diffuse fibro-purulent peritonitis ; spleen remarkably enlarged. The bacillus was to be seen in abundance on microscopic examination of blood from the heart, and was grown from thence in pure culture.

October 10*th*, 1891 : A small guinea pig was inoculated into the peritoneum with 0·1 cc. of the condensation water of a one day old agar culture, and died on the following morning with diffuse sero-purulent peritonitis, moderately abundant effusion, and a few fibrinous deposits upon the liver and stomach. The retroperitoneal and mesenteric lymphatic glands were somewhat reddened, but scarcely enlarged ; intestine normal. Pure cultures were obtained from the heart blood.

October 12*th*, 1891 : One drop of the water of condensation of a three day old agar culture was introduced into the anterior chamber of a rabbit. October 13th : the eye is much injected, hypopion. October 14th : the eye has suppurated completely. October 15th : the rabbit is moribund. The heart-blood contained abundant bacilli. Metastatic abscesses in the liver. The whole of the intestinal contents liquid. In the lower portion of the small intestine the mucous membrane was deeply reddened ; no evident local swelling of the follicles.

October 12*th*, 1891 : A small guinea pig received 0·3 cc. of the condensation water of an agar culture subcutaneously under the skin of the back. October 13th : the animal died this evening. The blood of the heart contained numerous bacilli in pure culture ; phlegmonous inflammation of the subcutaneous

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tissue of the back; serous peritonitis; no metastatic abscesses
in the viscera.

October 15*th*, 1891 : This afternoon the common duct of
a small dog was ligatured, and a syringe full of slightly
turbid washings, in sterilised water, of a three days old pure
gelatine culture was injected into the gall bladder.   The
puncture hole ligatured; disinfection; gastrorraphy. Tempera-
ture, October 15th, before the operation, 38·2° C.   October 16th,
morning, 39·7°; mid-day, 40°; animal very feeble, and timid;
evening 40·4°.   On October 17th, death.

Autopsy : abdominal wound completely closed, no suppuration
in it; the heart-blood was inoculated from; it contained the
bacillus in pure culture.   In the heart there was much clot
and fluid blood; the curtains of both venous ostia showed
much œdematous swelling, were transparent and soft; in the
median mitral curtain also there were numerous small puncti-
form hæmorrhages, but no conspicuous deposit; lungs airless,
showing no inflammatory foci; abdominal viscera dry, intestines
pale and contracted, no diffuse peritonitis; transverse colon
adherent to under surface of liver, and drawn up towards
the gall bladder, as also the duodenum ; gall bladder full and
distended, and attached by slight fibrinous adhesions to the
adjacent lobe of the liver; no pus anywhere; the spots of
ligature intact.   From the bile the bacillus grew in pure
culture; it can be recognised in the fluid by means of the
microscope without staining.

On the surface of the liver were yellowish white foci of
suppuration of the size of a pin's head, and the same were seen
in sections, being about equally numerous in all the lobes.
The intrahepatic ducts were somewhat dilated, but their mucous
membrane was not affected.   The spleen much enlarged, has a
marbled appearance, bluish-black prominent portions alterna-
ting with depressed paler areas.   On section the prominent
portions turn out to be hæmorrhagic infarcts.

In dog's bile, fractionally sterilised, the bacillus grew at the
body temperature, and showed no modification of form.

In the fourth and fifth cases practically the same bacillus was
found.   The growth on potato was not tried in them.

Probably in all these cases which I examined and also in
those of Netter and Martin, Girode and Gilbert, and Bouchard,

the organism present was the notoriously variable *bacterium coli commune*. Moreover, this bacillus is undoubtedly derived from the intestine, it is certainly pathogenic, and is especially capable of exciting cholangitis and cholecystitis. Nevertheless, stagnation of the bile apparently favours its action, for whereas it produced the most acute infection in the biliary passage of a dog after ligature of the common duct, and quickly destroyed the animal, the injection of a similar culture into a dog, apart from ligature of the duct, produced no symptoms whatever, and when the animal was killed eight days later nothing abnormal was found in the biliary passages or liver.

It is known that many bacteria can make their way into the bile from the blood. Such transit of the glanders bacillus has been described by Farraresi and Guarineri ; of the cholera bacillus by Nicate, of the bacillus of spleen fever by Oemler, Strauss and Chamberland, of the rinderpest bacterium by Oreste, of the *diplococcus pneumoniæ* by Pernice and Alessi, of Friedlander's bacillus by Bernabei. However, Bernabei could only confirm the statements of the earlier authors referred to as far as the bacillus of the rinderpest is concerned.

Apparently such invasion of the bile from the blood has no importance in connection with the ætiology of cholelithiasis.

The frequent occurrence of *bacterium coli commune* in the biliary passages in cholelithiasis suggests the question whether the disease is not the result of the introduction into them of this microbe.

In the first place, the organism may be the cause of the deposition of bilirubin-calcium in the biliary passages. Putrefactive micro-organisms at any rate appear to do this, for one frequently sees deposits of bilirubin-calcium in the spots in which colonies are growing in decomposing bile.

Furthermore, in one gall bladder, I found four small, hard, irregularly-shaped black stones, little larger than a millet seed, which consisted for the most part of bilirubin apparently in a free state. After I had extracted most of this substance by means of alkalies, there remained a brown substance, which still retained the form of the little stone. In this there were included rather thick, short rods, of the form of the above described bacillus, and frequently occurring as diplo-bacilli. Attempts to stain them with methylene blue were fruitless.

Against this view, however, is the fact that I have, as a rule, failed to find any traces of this bacillus in the newly formed concretions, and at any rate only the formation of bilirubin-calcium stones, and not that of cholesterin stones, can be so explained.

Much more probable is the view that the disease of the mucous membrane of the gall bladder, which leads to calculus formation (the stone forming catarrh), is a sequel of an invasion of the *bacterium coli commune.*

In contradistinction to the above is the explanation, which is likewise a possible one, that the lesion of the mucous membrane is to be regarded as a direct result of the stagnation of the bile, *i.e.,* of the injurious action of the bile upon the living tissues, but in favour of the latter explanation nothing further can be urged. That the invasion of the bacillus brings about cholelithiasis is by no means proved as yet; but I think that the following observation is best explained on this supposition.   In any one gall bladder the stones are usually, as Hein and Bramson have already pointed out, of quite uniform character and, as I believe any one who has a knowledge of the subject will agree, of about the same age.

Hence it would appear that the *formation* of gall-stones is a transitory occurrence, however chronic the resultant chole-lithiasis may be.

If this be so, stagnation of the bile, as such, can hardly be the cause of gall-stone formation, since it is the result of causes which are chronic in their action.

The invasion of *bacterium coli communis* constitutes, at any rate, an occurrence to which stagnation of the bile can occasionally lead, and which is capable of producing cholangitis and cholecystitis; and these again may give rise to the formation of gall-stones, and to cholelithiasis.

2. SPECIAL ÆTIOLOGY OF CHOLELITHIASIS.

(*a*) Diseases of the liver are among the causes of the production of bilirubin-calcium calculi in the intrahepatic ducts. These are undoubtedly more frequently met with when there exists local or general jaundice, as the result of connective tissue increase (cirrhosis) or new growths (syphilis, carcinoma).

(b) Local lesions in and about the large bile ducts, which lead to biliary stagnation, are very important causes, and in this group may be included tension on the cystic duct in connection with floating kidney, floating liver, and the liver of tight lacing, which has been fully discussed on page 40.

(c) *Cholangitis.*—The important part which cholangitis, following upon stagnation of bile, plays in the ætiology of cholelithiasis has been set forth on p. 46. But cholangitis also occurs without obstruction, as in typhoid, diphtheria, &c. That such cholangitis also leads to the formation of concretions has not been proved, but is highly probable.

(d) *Foreign bodies.*—The occurrence of foreign bodies in gall-stones has already been mentioned in Section I., 6c. One should not look upon the formation of gall-stones around such foreign bodies, as simply due to the precipitation from the bile of cholesterin and bilirubin-calcium upon them, as points of crystallization. The fact is that the foreign bodies cause disease of the biliary passages by giving rise to obstruction, injury, and infection. It is only as a result of such disease that the cholesterin and bilirubin-calcium are produced, which then collect around the foreign body.

Among foreign bodies gall-stones themselves play much the most important part. They continuously injure the mucous membrane, and give rise to obstruction and thus favour the disease directly, and also by constantly repeated opportunities for infection, as hardly anything else does.

The small intrahepatic bilirubin-calcium stones occupy a quite peculiar position. They appear not unfrequently to play towards the gall bladder the part of foreign bodies, and so set up cholelithiasis.* Remarkably frequently, at any rate, one finds such calculi, derived from the hepatic ducts, as nuclei of cholesterin stones in the bladder.

I possess several sets of as many as twenty to thirty stones out of one gall bladder, in the centre of each of which is a small bilirubin-calcium calculus.

(e) In pulmonary tuberculosis, and in connection with cir-

* Thudichum has stated that in the centre of most gall-bladder-stones casts of the hepatic ducts are to be found, and he holds that such casts usually form the nuclei of crystallization of the concretions in the gall bladder ; from the pictures which Thudichum gives of his bile duct casts, I can only say that I have never seen such.

culatory disturbances gall-stones appear to be common.   Still
the fact is doubtful, and the casual relationship very obscure.

(f) The statement of J. Kraus is interesting, who states that
he has observed cholelithiasis in association with renal calculi
in forty-two cases.

If there is actually a connection between the two diseases, it
might be due to the hindering of the bile flow as the result of
the affection of the (right) kidney, or an infective influence
might be conducted from the diseased (right) kidney to the bile
passages.

I can only remember to have seen renal and biliary calculi
associated in one single case, and among the large number of
post-mortem records of patients who have died with cholelithiasis
which I have gone over, I have only in three or at most four
cases found the simultaneous presence of renal calculi noted.

The collectors of statistics, from Fielder down to Schröder
and Roth, none of them make any mention of any frequent
association of renal and biliary calculi.

CHAPTER VII.

SYMPTOMS OF CHOLELITHIASIS.

Cholelithiasis is only revealed by phenomena which are directly or indirectly due to the presence of gall-stones, and the process of their formation does not give rise to any symptoms. It is true that Kraus has recently described a " prodromal stage of cholelithiasis," but I recognise in his description merely the manifestations of chronic dyspepsia. Such dyspepsia may be a sufficiently frequent cause of the formation of gall-stones, but on the other hand it often enough does not produce the result. Certainly in the majority of cases gall-stones are formed and produce their peculiar effects, without a single antecedent symptom which points to their development.

Indeed, Kraus's standpoint is based upon the generally accepted notion that the formation of gall-stones is a process which reaches its completion slowly and gradually, extending over years, or at any rate many months. This appears to me to be by no means an established fact. No doubt calculi with crusts consisting of numerous laminæ require a considerable time for such layers to form. Again, the process of infiltration with cholesterin takes some long time; nor can we deny a considerable age to the crystalline " Solitären," but it seems quite impossible to define accurately what should here be understood by the term "a considerable age."

On the other hand it appears to me very doubtful whether the ordinary gall-bladder-stones, mixed bilirubin-calcium stones, and pure bilirubin-calcium gravel cannot be formed with great rapidity, and indeed I believe that such is the case.

The soft bases of calculi must obviously be of quite recent formation, and the earlier processes which imparts to them greater solidity can doubtless be very quickly completed ; since, if this were not the case, such soft bases would be readily broken up again, or dissolved by the freshly secreted bile in which they are bathed.

According to my belief these processes require no very long time for their completion, and it is quite possible that they are completed in the course of a few days or even hours.

Cholelithiasis is, as post-mortem observations show, an extra-ordinarily common malady. On an average every tenth human being, and of elderly women perhaps every fourth, has gall-stones. This does not of course express the frequency with which biliary calculi give rise to morbid phenomena, for one often enough finds, post mortem, the gall bladder and bile ducts completely packed with calculi, although these have never caused any inconvenience or produced any ill effects. In such cases cholelithiasis may be a perfectly harmless condition, and not merely a latent one.

We shall learn to appreciate the distinction between the above terms; for calculi may remain latent, although they have for a long time been anything but harmless, having already caused irreparable damage.

On the other hand, cholelithiasis does not usually remain absolutely harmless in the long run, because the concretions tend to increase in size. Sooner or later they produce ill effects, unless the patient dies too soon, or unless they, having previously been rendered innocuous, are got rid of. Such a result may be brought about in two ways, either by their being expelled without trouble and without doing harm, or by their being broken up again.

Evacuation of calculi, apparently *per vias naturales*, without symptoms or sequelæ has been frequently described. P. Frank has observed such cases, and I myself have also met with them. As a rule, however, in such cases the passage of stones without discomfort is the result of the previous passage of stones with discomfort, and in my experience this has always been the course of events. We shall see later that this is easy to understand, since after calculi have once passed along the bile ducts a dilatation persists which greatly facilitates the passage of after-coming stones.

It is certainly not a common event for the cure of cholelithiasis to be brought about by the painless evacuation of all the stones which have been formed. This can only happen when all the stones are very small and very soft, neither of which conditions is common, since they rapidly increase both in size and hardness.

The dissolving up of concretions once formed certainly plays no conspicuous part in the cure of cholelithiasis. One not unfrequently finds traces of a solvent action upon the calculi, and

among the many thousands of calculi which I have examined from this point of view, in some few dozens perhaps the process had proceeded far enough to render it probable that the calculi would actually break up. In all such cases a few isolated stones, amongst a number in the gall bladder, had undergone a solvent action, whereas the great majority remained intact.

On large single stones either of the cholesterin or bilirubin-calcium variety I have only very seldom found traces of solvent action.*

Gall-stones first betray their presence and produce their earliest morbid symptoms when they become impacted in the bile-ducts, or when they, whether so impacted or not, give rise to mechanical or infective lesions of the biliary passages.

To be sure, one often sees, in persons who are afterwards attacked with undoubted cholelithiasis, ill-defined symptoms preceding the attack by a considerable interval, such as enlargement of the liver, slight transitory jaundice, or trifling pains in the hepatic region, but such symptoms may very well be the results of the passage of very small, and probably soft, concretions along the bile ducts, in which they become impacted for a time. As far as I can see, one is not justified in referring such disturbances to the mere presence of calculi as such.

Later on we shall frequently have occasion to refer to the fact that concretions which are at rest in the biliary passages may reveal their presence by producing fever, and especially attacks of an aguish type. It is certain that this may be the case apart from any obvious complications. Probably an infective cholangitis exists in all such cases. As a rule, then, cholelithiasis first declares its presence by producing symptoms of impaction, viz., gall-stone attacks.

The impaction of stones occurs during their passage along the bile ducts, which usually ends in their exit into the intestine. The removal of calculi in this manner may be regarded as the regular course of cholelithiasis.

It is convenient, then, to describe as regular cholelithiasis the familiar, and, on the whole, highly characteristic group of symptoms which correspond to this regular course of the disease. In contrast to this is irregular cholelithiasis, which includes the

* Wyss believes that calculi are broken up by friction against their neighbours, but I have never met with any clear indication of this.

numerous secondary affections in and near the biliary passages, which are apt to ensue when the malady does not follow this regular course.

Naturally these two varieties of cholelithiasis may run into each other, for the affection may at first follow a regular course, and only assume an irregular form in its later stages.

A. REGULAR CHOLELITHIASIS.

This, then, is the regular course of cholelithiasis, that the concretions traverse the bile duct and enter the duodenum without doing any considerable amount of permanent damage. The resistance which they meet with in their passage has to be overcome by force, and this event manifests itself as gall-stone attacks, of which gall-stone colic is at once the most familiar and most characteristic form.

Gall-stone Attacks.

Gall-stones may remain at rest in the gall bladder for a long period, and it is not easy to say in what way they are suddenly set in motion in the end.

We recognise the passage of a calculus out of the gall bladder and its entrance into the cystic duct by the occurrence of an attack. Errors of diet are conditions which are known to frequently start such attacks, and many patients can reckon on the occurrence of one as the result of quite slight deviations from a most rigid dietary ; such, for example, as the indulgence in small quantities of spirits, beer, or wine. Chills are credited with a similar power, as also are emotional disturbances, strains due to stooping or lifting, and jolting of the body, as in driving or riding. Not unfrequently the earliest gall-stone attacks follow a few days after a confinement, or the removal of abdominal tumours by operation (Freund, quoted by Kraus). Moreover, women not unfrequently state that attacks repeatedly occur at the commencement of a menstrual period.

I will here briefly relate a case in which I was able to confirm this by observation :—

CASE I.—A girl, aged 18, who had previously enjoyed good health, suddenly experienced on September 20th, 1891, an acute pain in the right hypochondrium, radiating thence over the thorax, and accompanied with severe bilious vomiting. On the evening of the same day

menstruation commenced. On September 21st the pain and vomiting continued. On September 22nd jaundice appeared and remained very intense until the 24th. On September 28th very intense jaundice and severe pain in the hepatic region, coming on in paroxysms. The liver extended below the right costal border, its lower edge, which could be felt, being not particularly hard; it was tender on pressure. The gall bladder was not palpable; the spleen was not enlarged. Pulse regular, 80. The stools were bile-free. Under treatment with Carlsbad water the pains ceased on October 3rd, the liver decreased in size, the stools contained bile, and the jaundice had entirely disappeared. The urine no longer contained bile; the patient had regained her normal health.

On October 12th the catamenia returned (ten days too soon), and a few hours later there was a fresh acute attack resembling the previous one. On October 13th there was fresh jaundice, and the urine contained bile pigment. The liver was again swollen, palpable, and tender on pressure. The stools were not entirely decolorised. The pain, jaundice, and swelling of the liver lasted until October 20th, and then rapidly cleared up. On October 25th the patient was discharged quite well.

There was at no time any fever. No gall-stones were found, but owing to the patient's fault the motions were not regularly examined.

Gall-stone attacks also occur as complications of many diseases which are associated with intestinal irritation. Thus I have seen them in three cases of enteric fever during the early weeks, and in one of them stones were passed. Hagenmüller has collected as many as eighteen cases of enteric fever with gall-stone colic (Paris correspondence, *British Medical Journal*, 1885, p. 83). Lebert performed the post-mortem on a case of arsenical poisoning in which a freshly impacted gall-stone was present in the cystic duct.

These observations render it very probable that peristaltic disturbance of the intestines favours the setting in motion of previously quiescent stones.

The attacks often commence at about midnight, but no conclusion can be drawn from this fact as to the processes in the bile ducts which start them. Yet at about this time intestinal digestion is in active progress, and this observation does not appear to me to be in contradiction to those just mentioned.

Since, then, the bile ducts appear to share in the active movements of the intestine, we have every right to assume that at the same time as the ducts are the seats of a lively peristalsis a calculus may, by chance, become imprisoned in the neck of the bladder. As a result, reflex contractions of the

bile ducts are set up, such as will be discussed in later sections, and these drive the stone deeper and deeper into the cystic duct. When this happens the attack is definitely started. If the reflex spasm ceases in the muscular coat of the gall bladder before the stone had become impacted in the cystic duct, it may fall back into the cavity.

The calculus can hardly make its way into the cystic duct by any other means than through such peristaltic contractions of the wall of the gall bladder in the region of the duct, as, for example, through a simple dilatation of the bladder as it becomes filled, since the lumen of the cystic duct is too narrow. Even a concretion as large as a hemp seed can only be pressed into the duct by the exercise of considerable force.

Moreover, the cystic duct after its emergence from the gall bladder usually at once takes a turn upwards (*i.e.*, towards the fundus of the bladder). In this part of its course it is often
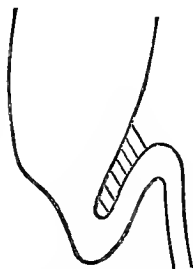
attached to the gall bladder by a kind of short mesentery, or is even closely adherent to its very wall. As a result the duct must actually be compressed when the gall bladder is fully distended, with the result that it can only be opened up by means of a muscular contraction.

General Pathology of the Attack.

The conditions upon which the character and severity of gall-stone attacks depend are the following—

1. The amount of resistance which the concretions encounter in their passage along the bile ducts is dependent upon :—

   (*a*) The width of the lumen and course of the bile ducts, and the presence of narrowing, winding, or bending.

 (b) The expansibility of their walls and the occasional occurrence of reflex muscular contractions in them (spasmodic stenosis).

 (c) The size, consistence, and form of the calculi.

2. The resistance may be overcome by—

 (a) The flow of bile.

 (b) Muscular contraction of the duct-walls, which pushes forward the stone which they embrace.

With regard to 1 (a). It has long been generally recognised that in the first place the cystic duct, and secondly the intestinal portion of the common bile duct must, on account of their narrow calibre, offer most resistance to the passage of gall stones. One can easily convince oneself that this is so, if in the cadaver one presses a gall-stone of sufficiently small size out of the gall bladder and onward into the duodenum. Whereas forcible pressure is required to drive it along the cystic duct, a less pressure suffices to move it along the common duct. Arrived at the intestinal portion of the duct it sticks fast, and more forcible pressure must be again employed to expel it.

In the case of stones originating in the hepatic ducts, only the obstruction of the outlet of the common duct has to be encountered; the remainder of the common duct allows sufficient room for its passage, since it is wider than the main hepatic duct.

With regard to 1 (b). In the cadaver the walls of the bile ducts have very little tendency to yield, and even a pressure sufficiently great to tear them is incapable of producing any considerable dilatation. In life, however, the walls of the bile duct appear to be less unyielding. I have found at any rate that in a small dog, recently killed, a calculus could be pushed along the common duct with comparatively little pressure, which could hardly be forced through the much wider duct of a human being.

Reflex contractions of the bile ducts undoubtedly occur. Laborde has produced such contractions experimentally in dogs, and stated that he has seen the walls contract upon a body introduced into the bile ducts and grip it tightly.

My own observations upon this point are given under 2 (b).

With regard to 1 (c). It is obvious that the hardness of the concretions is a factor of the greatest importance. In the gall

bladder and in the hepatic ducts pultaceous precipitates of
bilirubin-calcium are often met with, the passage of which can
hardly be more difficult than that of inspissated bile, and even
actual concretions are often so soft and friable that their passage
along the bile ducts can be effected without any great force. Such
is the case with freshly formed gall-bladder stones with thin
crusts and soft or even liquid nuclei, and with the majority of
bilirubin-calcium stones, and especially those derived from the
intrahepatic ducts. Even harder calculi appear to be capable
of being broken up in the bile ducts. At any rate small chole-
sterin calculi, of the kind described on a previous page, which
have already acquired a fairly thick, solid crust, and in the dry
state are so hard that they can hardly be crushed between the
fingers, are occasionally passed in fragments in the motions;
and it cannot be supposed that these have only been broken
up in the intestine.

In shape, calculi, which are not yet too large to pass the bile
ducts, are usually approximately spherical, or cubical or many
sided, with no considerable inequality of the various axes.
Nevertheless, stones of very irregular forms with long, pointed
processes do occur, but it is not my impression that such
irregularly pointed stones are responsible for exceptionally
severe attacks. On the other hand, it is obvious that the calculi
are very seldom so truly spherical that they accurately and
completely close the lumen of a duct, and we may readily
suppose that the angular and pointed form favours the passage
of the bile over the impacted stone. It is also of importance
as determining the character of the symptoms, whether a
calculus with marked inequality of development in its different
dimensions becomes fixed in its longer or shorter axis. Thus
the turning of a calculus may suffice to arrest the flow of bile
which was previously free, or may on the other hand serve to
set free a stone which was previously fixed.

With regard to 2 (a). Among the forces which drive forward
the concretion, the first place must be assigned to the flow of
the bile.

The secretion of bile takes place under a low pressure. In
dogs, according to Haidenhain's estimates, the secretory pressure
varies between 110 and 220 mm. of water, and we have no
reason for supposing that it is conspicuously higher in the

human subject. In the long run the pressure in the biliary passages can rise no higher, since when the pressure within them is higher the secretion of the bile is arrested, and that which has already been secreted is reabsorbed.

So low a pressure as this cannot suffice for the propulsion onwards through the narrow portions of the biliary passages of any but quite small concretions. In the case of a dead dog, with still distensible duct-walls, a far higher pressure, of at least 500—600 mm., of water was required to drive forward a stone of such size that it only became actually fixed in the common duct.

Very probably temporary elevations of pressure in the biliary passages, considerably in excess of the ordinary secretory tension, may be brought about by contraction of the gall bladder, but it would be incorrect to assume that the gall bladder can produce any noteworthy effects in this way sufficient to accomplish the expulsion of calculi which have become impacted. That it can so contract is beyond question, but the force with which such contractions take place must fall far short of what is requisite to produce the necessary elevation of pressure.

I have not succeeded, any more than any other experimenter has done, in producing, by any means whatever, energetic contractions of the gall bladder capable of manometric measurement.

In cases of gall-stone colic with palpable gall bladder we ought to be able to feel any powerful contractions thereof, such as one recognises so clearly in distended intestine, but, as far as I am aware, no one has ever observed them. I have only in one single case (No. XVI.) noticed anything of the kind. It appears to me, after what has been said, at least improbable that the bile stream any longer comes into play as a propelling force, when the stone encounters any considerable resistance in its passage.

The permanent rise of pressure in the biliary passages which only comes into play if the outflow of bile is arrested for a long time has quite another significance. Such increase of pressure, however slight it be (and it cannot greatly exceed the secretory tension, *i.e.*, 200 mm. of water), cannot be without effect in the propulsion of calculi, since it produces lasting dilatation of the entire system of bile ducts.

Such dilatation of the ducts is very frequently observed in cases in which cholelithiasis exists or has existed, and it even appears to be developed in cases in which there has been no long standing jaundice; at any rate I believe that I have certainly seen one case of the kind. Moreover, this is quite intelligible, for the impacted stone will at first close the duct, and as a consequence the pressure in the bile passages will rise, with the result that the lumen of the duct is widened, so that the bile is again able to flow between the calculus and the duct-wall. Again, very small and soft concretions, which do not become actually impacted in any part of the ducts, and even inspissated bile, may, of course, produce the same result.

Transitory elevations of pressure of very considerable degree can, as will be evident, and as one can observe in animals by means of a manometer tied into the gall bladder, be brought about by pressure of the abdominal walls, but nevertheless it is highly improbable that such abdominal pressure plays any important part in the expulsion of impacted calculi. I have never observed that the patients make any instinctive use of abdominal pressure during their attacks.

With regard to 2 (*b*). In the expulsion of calculi, the effective diameter of which markedly exceeds that of the lumen of the duct, the contraction of the muscular coats of the bile passage plays a conspicuous part. The statements of authors regarding the presence of unstriped muscular fibres in the walls of the bile ducts are not in complete accord, so I forbear to discuss these statements. One can easily convince oneself of the occurrence of peristaltic movements in these structures in the case of birds. Hyrtl mentioned these in his *Topographic Anatomy*, and in Stern's experiments on pigeons they were constantly seen. In mammalia I have never observed them, but, on the other hand, in rabbits energetic reflex contraction of the common duct can easily be excited. The rabbit is operated upon without an anæsthetic, and after the abdomen has been opened the common duct is brought into view by drawing forward the duodenum. Electric stimuli applied externally to its wall produce no effect, but when one electrode is introduced into the duct from the duodenum, the interrupted current always causes a contraction. Curiously enough this contraction is greatest, not at the actual point of stimulation, but about half to one centimeter above it.

At this point it is always so pronounced that the lumen of the duct is obliterated. If the stimulation be long continued, the contraction persists for minutes together, and always considerably outlasts the stimulus. I have never seen it advance as a peristaltic wave, either towards the duodenum or towards the liver.

So far as what has thus been observed in rabbits may be supposed to hold good for human beings also, we here make the acquaintance of a process which is of very great importance in the propulsion of large calculi along the biliary passages. The impacted stone irritates the mucous membrane just as the electrical stimulus does, and since the reflex contraction of the walls takes place above the calculus, the coats of the duct will be, by this means, drawn away from the stone towards the liver, whilst the stone itself is at the same time moved onwards on its way towards the duodenum. In dogs I have never been able to excite contractions of the bile ducts, probably because I have only experimented upon them under an anæsthetic. Laborde has observed powerful contractions in dogs which were not anæsthetised, and he also failed to obtain them when the dog was rendered insensible with morphia or chloroform. The following is an interesting experiment of Laborde's. He introduced six small gall-stones into the common duct of a dog from the duodenum, and at the autopsy four of these lay in the intestine, and two others in the gall bladder.

The violent contractions of the duct-walls, which are capable of pushing the calculi forwards, are the cause of the pains of biliary colic; these are, indeed, in their mode of origin, true colic pains, as has long been generally recognised.

In one of the experiments on rabbits above referred to the blood pressure in the carotid was recorded by means of the kymograph. Stimulation of the common duct exercised no recognisable influence upon the blood pressure or upon the frequency of the heart's action, either in curarised or noncurarised animals. Simonoffski, on the other hand, has obtained conspicuous elevations of blood pressure by electrical stimulation of the gall bladder, even of curarised animals (from 114 to 128 mm. of mercury in the carotid). The rapidity of the heart's action rose at first, but fell again with increase of stimulus, and ultimately the action became irregular.

5

2. *Symptoms of Gall-stone Attacks.*

Gall-stone attacks present, in typical cases, a very character-istic group of symptoms, viz., pain, vomiting, jaundice, and febrile disturbance, together with tenderness and swelling of the liver. Of these symptoms the pain is by far the most important. It is seldom wanting, and is often of the colic type, and thence it is that the attacks are universally described briefly as gall-stone colic. The typical attack commences with, or is quickly attended with, intense pain. The patient shivers ; the shivering increases to an actual rigor, followed by a hot stage, and sometimes, though more rarely, by sweating. Then follow nausea and vomiting, which, by producing exhaustion, gives rise to a deceptive appearance of quiet and amelioration. With temporary remissions the painful condition not unfrequently continues for hours, and often enough for days together. Then it sometimes comes to an end with characteristic suddenness, often only to return in the course of some hours or days. Usually the relief is not so immediate, but follows a period of diminished pain, which persists for hours, days, or even weeks together with now and then a recurrence of the acute symptoms, until at length, after or apart from such a relapse, it gives place to a condition of ease. When much enlargement of the liver or jaundice is present, a number of days at least elapse before this passes away.

3. *Details of the Attack.*

The attacks often come on without any particular exciting cause, but very frequently such causative factors as have been referred to may be recognised. The first commencement of the pain often occurs at midnight, and in my experience this has been specially the case with first attacks of colic. Again, the attacks more frequently begin during the afternoon and evening than at other times of the day. In the majority of cases premonitory symptoms are present. For some hours, and often even for a few days, before the actual attack the patients experience uncomfortable sensations in the epigastrium ; they may shiver, and may even be already slightly jaundiced, and suffer from cutaneous itching. The liver may be already

swollen and painful on pressure. These premonitory symptoms very probably indicate the passage of concretions of the very smallest size, which do not become actually impacted, but which produce motor disturbances in the bile ducts, and so lead to the passage into them of larger concretions, which then become impacted. In many cases, however, impaction, attended by its most severe manifestations, develops suddenly upon a condition of complete well-being.

The Individual Symptoms.

As has been already mentioned, pain is by far the most important symptom, and it is wont to be the earliest of all the more severe manifestations.

The pain of biliary colic is often of excruciating severity, so that the patients usually speak of it as " unbearable " or " deadly," and it calls forth cries of suffering even from the bravest. Women who have borne children often declare that labour pains are easy to bear in comparison to these. Sometimes the pain is of a colic type, cutting, boring, or tearing in character ; sometimes it persists for a quarter of an hour or more with unlimited severity, and then comes a temporary alleviation, followed by a fresh exacerbation, and this is the course of events for days and nights together. In many cases, however, the pain is not so intense, and occasionally is quite insignificant, amounting merely to a slight sensation of burning, gnawing, or pressure.

The pains usually commence in the epigastrium, and afterwards spread into both hypochondria and to the back, where they are often felt not only to the right, but on both sides of the vertebral column. Sometimes they extend upwards to the head and neck, or downwards to the lumbar, and even to the sacral region. Now and again they radiate into the upper part of the thigh, and along the arms even to the finger tips.

Pain in the right shoulder is not, in my experience, by any means especially common in gall-stone colic, and is relatively much less frequent than in cases of hepatic abscess.

The pain of gall-stones is in the great majority of instances characterised not only by its intensity, but also by the further fact that its point of maximum intensity is in the hepatic

region (hypochondrium). It is far from common for it to be more severe in the left than in the right hypochondrium, and actual limitation to the left hypochondrium, with complete immunity of the right, is a condition of the greatest rarity. I have only seen one such case.

CASE II.—A lady, in her thirtieth year, and well nourished, had suffered for two years from attacks of pain. These usually occurred at night, but sometimes in the afternoon also. The attacks, which were of great severity, were attended with bilious vomiting, and sometimes with rigors and elevation of temperature. The pains had their seat in the epigastrium and left hypochondrium. The patient was very sceptical as to the diagnosis of gall-stones, since she repeatedly declared that never in any one of her attacks had she suffered from pain on the right side. After a course of Carlsbad waters was initiated, five small, facetted gall-stones, of the size of peas, were soon passed during an attack.

The pains often radiate to the hypogastrium, but the patients are always able to state that they originate in the upper part of the abdomen. Of extension into the external genital organs or into the perineum, such as is often present in renal colic,* I have never got more than very questionable accounts: it is certainly very rare. On the other hand, complaint of pains radiating into the arms or legs is by no means very uncommon, and in some instances the attacks have commenced in the legs or arms.

Spasmodic muscular contraction (reflex spasms) sometimes develop.† These manifest themselves, when the pain is at its height, as cramps, *i.e.*, intensely painful tonic spasms of the muscles of the legs, or more frequently of the hand and finger muscles. Clonic spasms have also been described. In the often quoted and peculiar cases of Duparcque the condition was obviously one of hysterical convulsions.

Among the reflex spasms contractions of the abdominal muscles are of course included.

As a matter of fact these often occur in gall-stone colic, being more marked upon the right side, and by no means rarely con-

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* I can only find record of acute pain conducted into the penis in a single case of Trousseau's, quoted by Fauconneau, p. 195.

† Trousseau has observed reflex-paralysis (paraplegia) as a sequel of gall-stone colic (*Clinique de l'Hôtel Dieu*, vol. iii.). The case which he records will appear a very doubtful one, even to those who look upon the occurrence of reflex-paraplegia as an established fact.

fined to that situation. They are often completely involuntary, and occasionally occur apart from any acute pain or any considerable tenderness of the liver on pressure. In such cases they are, as Graves long ago pointed out, important aids to the diagnosis of liver affection. Such contractions of the abdominal muscles are said to be very painful, and, according to some observers, are the chief cause of the pains of gall-stone colic. I have not been able to convince myself of the truth of either of these statements, and I am unable to accept the latter view, seeing that with acute pains the abdomen is at times quite soft and the liver readily accessible to palpitation. As a rule the pains are rather due to a contraction of the muscular walls of the bile ducts around the impacted stone, excited by the irritation of the mucous membrane in its neighbourhood. Again, in some cases acute enlargement of the liver, and in others acute (cholecystitic) swelling of the gall bladder, contribute not a little to the severity of the pain.

2. *Vomiting.*—Very frequently, and in severe cases almost invariably, the pains are accompanied by vomiting. This is very persistent and severe, and thus contributes materially to the sufferings and exhaustion of the patients. Effectual vomiting produces only a temporary relief if the stomach be full; and if it be empty the vomit is usually only scanty, is almost invariably rich in bile, green, and of a bitter taste. Sometimes round worms are present in the vomit, but fæcal vomiting has never occurred in my experience, however severe the vomiting, unless intestinal obstruction existed.

Gall-stones have frequently been vomited during attacks * (Petit, Fauconneau-Dufresne, Cyr, Murchison, Harley, Thudichum, Pope, Kraus, Van der Byl, and others). The fact that bile is almost always present in the vomit is not without significance, since it shows that the bile has free exit through the common duct. The bile is of course derived from the duodenum, and in the same way gall-stones which are vomited can enter the stomach through the pylorus, and it is not necessary to conclude from their presence that a perforation exists between the biliary passages and the stomach. This is proved by Van der Byl's case, in which a gall-stone was vomited during life, and post-

* *Memoires de l'Academie Royal de Chirurgie,* 1743.

mortem a fistula between the gall bladder and duodenum was found.

3. *Fever.*—Gall-stone attacks often run their course without any subjective or objective febrile symptoms, but in some instances fever plays a conspicuous part. The pains are frequently accompanied by a rise of temperature, and the temperature may rise to 104° or more, apart from rigors or any other febrile phenomena; but a feeling of heat is usually present. Very commonly severe rigors accompany the colic attacks. In such cases there is always a rise of temperature to 104° or higher, and even to 106°. The cold stage is followed by a hot one, but sweating is often absent. As a rule the entire febrile attack does not last long, not more than a few hours, but I have seen one case in which after each rigor the temperature remained up for, twenty-four hours or longer.

The onset of a rigor not unfrequently anticipates the pains.* These febrile attacks accompanying the colic are probably excited by the irritation of the biliary mucous membrane; and as Budd, Frerichs, and more recently Schmitz, have held, they may be compared to the febrile disturbance following catheterisation of the urethra, and may be designated reflex fever.

I append the notes of a case which affords a very characteristic example of such colic-fever.

CASE III.—A workwoman, unmarried, aged 21 years.

Personal History.—The patient enjoyed good health during her early years. During the past year she suffered for three weeks from acute pains in the right side, daily recurring rigors, during which the pains were more severe, and frequent vomiting, with deep yellow colouration of the sclerotics. After this condition had lasted for three weeks, the patient again felt perfectly well. On Sunday the patient was again attacked with severe pains in the hepatic region, moderately severe rigors occurred daily in which the pains were markedly intensified, and she vomited occasionally. The stools were somewhat paler than usual, but still had a yellow colour.

Present Condition.—Strongly built woman, sensorium unaffected. She complains of intense paroxysmal pain in the hepatic region; sclerotics slightly yellow; tongue moist, with whitish fur; lungs and

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* Pemberton (*A Practical Treatise, &c.*), who as early as 1820 described the frequent occurrence of rigors with biliary colic, stated that they always follow after the pain.

heart normal; abdomen somewhat tumid; abdominal walls fairly lax; hepatic dulness commences at lower border of fifth rib, and extends two fingers' breadth below the costal border in the nipple line. The organ feels hard, and even the slightest pressure upon it is intensely painful to the patient. There also occur spontaneously from time to time, over the entire hepatic region, intense boring pains of short duration; splenic dulness not increased; spleen not palpable; motions irregular; urine scanty, depositing a sediment of urates, sp. gr. 1020, free from albumen, and giving no bile-pigment reaction. Appetite bad; sleep sometimes disturbed by pains; was given Carlsbad (Mühlbrunnen) water to drink hot.

March 22nd: The pains could only be slightly alleviated by repeated injections of morphia, and at night they were again rather severe. The patient vomited early this morning after taking the Carlsbad salts. Appetite bad. The skin is to-day slightly yellow, and the
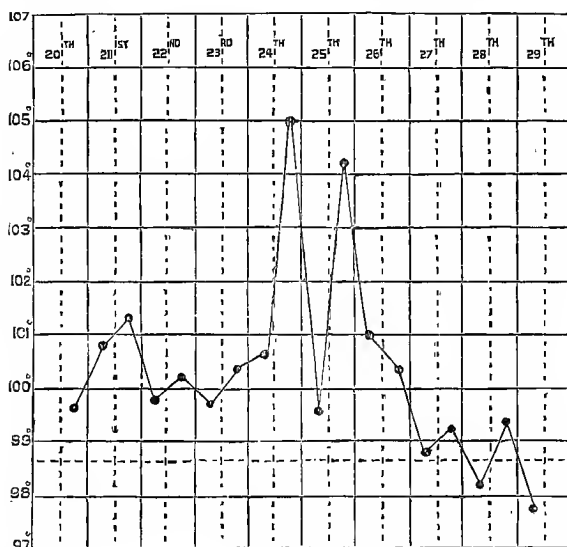
sclerotics are decidedly jaundiced. The urine looks rather darker, but gives no clear bile-pigment reaction. There have been about four loose motions, which had only a pale yellowish colour.

March 23rd: Icteric colour of the skin well marked; urine darker still, foam yellow, feeble Gmelin's reaction. The pains in the hepatic region have only ceased for an hour or two after the morphia injections, and to-day are again very severe. Vomiting occurred again to-day.

March 24th: The patient had a very severe attack of pain last night, which began with a rigor; after a small dose of morphia the pain was

somewhat less. Motions loose, of a faint yellow colour. Vomiting again occurred this morning. Appetite bad ; evident jaundice of the skin and sclerotics. The urine gives the bile-pigment reaction to-day.

March 25*th :* Yesterday afternoon the patient had a sharp rigor, which was followed by intense pains, which could not be relieved even for a few hours by moderately large doses of morphia, ·02 grm. Patient vomited. The stools continued to have a slightly yellow colour ; no gall-stones have as yet been found in them. Urine clearly icteric. Skin jaundiced.

March 26*ih :* Yesterday afternoon a fresh attack of severe pain commencing with a rigor, and the pains lasted through the night in spite of repeated injections of morphia, but were less severe than during the day-time. Examination of the pale yellow stools has to-day resulted in the finding of a gall-stone of the size of a pea with finely granular surface. To-day the patient is free from pain. Appetite worse. Jaundice pronounced.

March 27*th :* Patient is free from pain. Appetite somewhat improved. No further stones found in stool ; but a large round worm.

Maroh 28*th :* Patient has no more pain, feels better, and is beginning to regain her ordinary colour. The urine no longer yields a bile-pigment reaction. No gall-stones in stool.

March 29*th :* Condition unchanged.

March 30*th :* Patient already wishes to get up. Still some jaundice of skin and sclerotics. No gall-stones in stool.

March 31*st :* Conditions unchanged.

April 3*rd :* The patient has been up each day. She has continued free from pain, and has had a good appetite. Stools still free from stones, and deeply bile stained. Liver no longer tender on pressure. Skin no longer jaundiced, but sclerotics slightly yellow. Urine pale, free from albumen and bile-pigment. Patient was discharged to-day at her own desire.

We must distinguish from such colic-fever the " fièvre intermittente hépatique " of Charcot. This has its origin in the infection of the bile, which is especially apt to supervene in connection with biliary obstruction, and which has been already treated fully on p. 46. From the biliary passages the infection can easily become distributed over the organism, and this will be fully discussed in connection with cholangitis.

This biliary fever occurs not only with gall-stone colic, but also, although much more rarely, with obstructive jaundice of any origin. It presents itself as a condition of more continued, markedly remittent or intermittent, fever, either with quite

irregular exacerbations, occurring either at intervals of several days, or regularly every day, and often attended with rigors. Colic may be absent or may accompany each exacerbation. Acute enlargement of the spleen, which may attain to a considerable size, is often present.

CASE IV.—Field labourer, aged 48. Stated to have suffered from abdominal pain in 1883. In July, 1886, the patient was suddenly seized with acute abdominal pain, and felt very hot. On the following day he was said to have become yellow and to have vomited. The stools were white, the urine brown. It appears that the patient had continuous pain in the abdomen for four weeks, that the vomiting continued, that there was neither fevers nor rigors. The patient was ill eight weeks in all, but yet the jaundice appears to have only lasted four days. In February, 1887, there was a repetition of the attack,
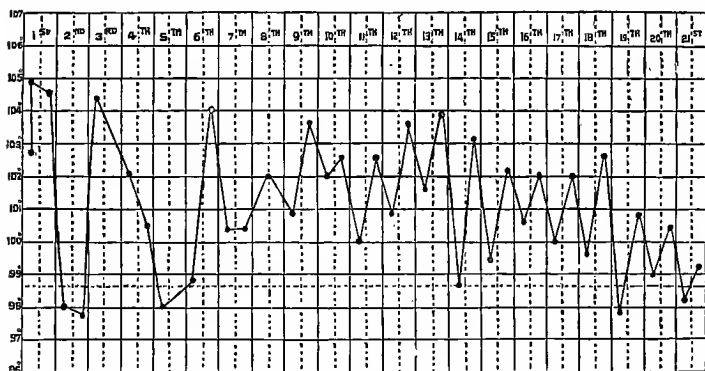
which, on this occasion, lasted fourteen weeks. The patient was again yellow, and there was high fever, rigors, and vomiting. Recovery was on this occasion very gradual.

The present attack dates from Monday, November 26th. He then felt a slight malaise, which increased on the Tuesday. He suddenly shivered and pain set in under the right costal arch, which radiated to about the *linea alba*.

On November 29th: The patient vomited for the first time, and the vomited matter was yellow. The vomiting occurred as soon as the patient took any food. On Friday morning the vomiting ceased.

November 29th and 30th: The pain again increased and became colicky.

December 1st, 1888: The patient gives the impression of being very ill. Very strong *fœtor ex nare*. Slight jaundice of the sclerotics.

Respiration 21.   Pulse 105.   Liver not clearly felt; hepatic region
tender.   Spleen greatly enlarged, hard, palpable for a hand's breadth
below the border of the ribs.   Vomit consists of slimy lumps.   Lungs
and heart normal.   Urine contains albumen 0·04 per cent.; specific
gravity 1027.   Microscopic examination of the blood showed nothing
abnormal.

December 2nd: A rigor.

December 3rd: A slight rigor and vomiting.   No evident slowing
of the pulse.   Respiration remains normal.   The jaundice is much
increased.   The urine is dark brown, gives a distinct bile-pigment
reaction, and contains traces of albumen.   The stools, which are still
hard, only followed upon an enema.

December 8th: Yesterday and to-day the bowels were opened spon-
taneously for the first time.   Motions contain bile, but no calculi.
The diaphragm lies very high; the abdomen is distended.   The apex
beat is felt in the fourth intercostal space, close to the nipple and on
its inner side.   Heart sounds normal.   The upper limit of the liver in
the nipple line, in front, is at the upper border of the fourth rib.   The
lower border of the liver as ascertained by percussion is in the nipple
line a little below the edge of the ribs.

December 10th: On December 8th a gall-stone a little larger than a
cherry-stone was passed in the motion, and the patient felt more easy
afterwards.   Since then no more rigors, but the fever continued for a
long time.   The jaundice and splenic enlargement gradually decreased,
and recovery took place.

The greater severity of the fever and its independence of the
colic attacks are very clearly shown in this case.   Moreover,
the fever outlasted the passage of the calculus by a number
of days.

It is by no means uncommon for patients with cholelithiasis
to be troubled with such fever, with rigors, for periods of many
months.   Such cases differ widely in their type, according as
the rigors are accompanied by colic and jaundice or no.   The
cases of the first kind will be discussed more fully in connection
with chronic gall-stone jaundice.   Cases of cholelithiasis with
long continued fever and erratic rigors, more or less resembling
an irregular ague, and unattended with colic attacks or jaundice
can easily be misunderstood; they are sometimes mistaken for
malarial fever.   Frerichs has briefly recorded a case of this kind
in which the stones were situated in the intrahepatic ducts,
and more recently Schmitz has described two similiar cases in
which also jaundice was wanting.   Schmitz calls attention to
the fact that in such cases, in contradistinction to cases of
malaria, even when actual colic is absent, the rigors are still

accompanied by certain unpleasant sensations, such as tightness or fulness in the epigastrium, which are here the equivalents of colic attacks. Moreover, the sensation of dragging and stretching in the limbs, which preceded the cold stage of ague, as well as the characteristic sweating stage, are as a rule absent.

In all these cases we are probably dealing with an infective and not with a reflex fever.

In favour of this view is the great improbability that the irritation of the mucous membrane by stones, which in most cases of this kind are stationary, is capable of repeatedly giving rise to similar reflex phenomena. The analogy of urethral fever cannot be urged in support of such a view, for, as Osler has pointed out, in that condition the fever sets in as the result of a single irritation or one a few times repeated, and not of one which is repeated indefinitely. Moreover, the considerations bearing upon this question, which are brought forward in connection with hepatitis and cholangitis, compel us to discard the theory of a reflex fever in such cases.

A very evil prognosis is attached by some authors, including Schüppel, to true biliary fever. This is certainly going too far, since biliary fever often runs a favourable course in cases in which it is dependent upon gall-stones; as, for example, when the calculi are passed or got rid of. It is true that this frequently does not happen, and then the course may be unfavourable.

Jaundice.—The frequency with which jaundice occurs in connection with gall-stone colic is variously stated by different authors. Whereas Wolff met with jaundice in less than half of his cases, all of which were confirmed by the finding of calculi in the stools, Fürbinger holds that it is only wanting in about a quarter of the cases. In this connection it is advisable that a distinction be drawn between cases of trifling and of conspicuous jaundice. In cases of the first kind the yellow colouration of the skin and Gmelin's reaction in the urine are doubtful, and merely slight yellowness of the sclerotics is present, whereas in those of the latter class the yellowness of the skin and sclerotics is conspicuous, and bile pigment is obviously present in the urine. According as authors include the cases of trifling jaundice or no, their results will vary, but I think one should not

include such cases, seeing that such slight jaundice is sometimes difficult of objective proof, and is, moreover, very common in many different affections of the abdominal organs, and is, at any rate, in no way characteristic of gall-stone colic. If one confines oneself to those cases in which the jaundice is conspicuous, *i.e.*, in which there is evident yellowness of the skin and sclerotics, or undoubted bile-pigment reaction in the urine, this symptom will, according to my experience, be frequently found to be absent, that is to say, in at least half of all gall-stone attacks. No doubt if the attacks frequently recur this important symptom will sooner or later put in an appearance ; but yet it often happens that a long series of attacks occur in the same patient apart from any jaundice. I had under my care a patient (the wife of a medical man) who had frequently suffered from gall-stone colic, extending over 8 years, without ever being jaundiced, but she ultimately had an attack attended with jaundice, in which a stone of considerable size was passed.

Trousseau once saw jaundice develop for the first time after the patient had passed through very numerous attacks spread over a period of 4 years. In one of Murchison's cases this symptom was permanently absent, although the patient had suffered from daily attacks of colic for 4 months. Chomel (quoted by Fauconneau-Dufresne) records the case of a patient who suffered from thirty-four severe attacks of gall-stone colic, in only two of which jaundice occurred, whilst three were followed by white stools.

Jaundice usually develops rapidly when it occurs, so that as early as 12 hours after the commencement of the attack (*i.e.*, the pains) it may have attained its full development. The urine still sooner becomes dark coloured and contains bile pigment; and there are, apparently, cases in which bile pigment is temporarily present in the urine, without the development of any obvious jaundice of the skin.

The jaundice requires different periods for its disappearance, according to the length of time that the impaction of the gall-stone lasts, and the degree to which it attains. Even when the impaction has lasted only a day or two, and the jaundice is barely " obvious," several days are usually required before the sclerotics again become white. As a rule it does not persist much longer than a week after the passage of the stone, except

in protracted cases, and even in these only when it has been very intense.

From the urine the bile pigment disappears more rapidly, often even after a single day, and under these circumstances the urine usually shows an increased excretion of urobilin. Rarely it happens that, even at the height of severe jaundice, the urine, although dark in colour, contains throughout only urobilin instead of bile pigment. I have seen this in one case of chronic jaundice from gall-stones.

Even when the jaundice is pronounced the stools are by no means always bile free (clay-coloured), and often enough they contain bile throughout, although the jaundice is severe. In other cases a single clay-coloured stool may be followed by one containing bile. This is sometimes a favourable sign, and may indicate that the stone has been expelled. But this is by no means always the explanation, for other clay-coloured motions may quickly follow. This may be explained by supposing that the stone has merely assumed a more favourable position for a time, so that it no longer completely obstructs the lumen; or that the duct behind the stone becomes dilated by the obstructed bile, and the stone is thus induced to allow its escape; but that when this has happened the duct contracts once more, and complete obstruction again follows. Lastly, one stone may have been expelled, and a fresh stone may have entered the common duct. When, for a number of days together, clay-coloured stools are passed which are quite bile free there exists an unusually obstinate occlusion of the duct, and the case is likely to run a tedious course.

Among the numerous phenomena which may result from jaundice, itching of the skin must be referred to. This is sometimes a very troublesome symptom in cases in which the impaction (jaundice) persists for some time. It must be looked upon as a result of the jaundice (an effect of the reabsorbed bile) although it sometimes commences before any visible colouration appears, as Murchison noticed, and as I myself have certainly observed in a few cases. When it has once put in an appearance it usually persists as long as the jaundice does, and in one instance I have seen it long outlast it. Certainly the cessation of the itching is sometimes the first indication that the patency of the duct is restored, and that the stone has been

expelled ; just as an increase of itching, when jaundice is already present, now and then heralds a fresh attack of colic and an increase of the jaundice.

The development of pronounced jaundice is a tolerably certain sign that the calculus is situated in the hepatic or common duct, usually in the latter; but its absence affords no clue to the position of the stone, which may remain for a long time in the common duct, and yet no jaundice develop.*

5. *The condition of the heart and circulation.*—The pulse rate is often slowed during the colic attack, but this cannot be in any way laid down as a rule. Its rate (Wolff, Kraus) sometimes falls to forty beats in the minute. By way of explanation Wolff has recalled attention to the fact that, as Turck observed, a similar phenomenon occurs during severe attacks of pain in neuralgia. If pronounced jaundice develops, the pulse rate may again become slowed, as a so-called cholæmic symptom. Circulatory disturbances, such as chilliness, formication in the hands and feet, a feeling of compression, cyanosis or collapse, are very common, and in severe attacks may constitute very prominent symptoms. Here we are dealing with reflex vaso-motor phenomena. On the other hand, although they occur in the young and in specially sensitive persons, they also occur in severe, and sometimes in alarming, forms in older persons whose hearts are feeble, and there play an important part in modifying the character of the colic attacks. In old people death has resulted from cardiac failure, as in a case recorded by Kraus. In one of the cases described under cholecystitis also such attacks of cardiac failure occurred.

6. Albumen often appears in the urine. It disappears with the cessation of the attack, and its occurrence is to be referred to disturbances of the renal circulations during the attack.

* At the time when this was written (in the year 1891) I was myself still too much under the influence of the then prevalent notion that the jaundice of cholelithiasis is dependent upon the fixation of a calculus in the common duct, although I sought even then to free myself from this idea (compare what is said regarding chronic jaundice from gall-stones on p. 99 and the pages which follow). At the present time I should prefer to state the matter as follows:—The development of pronounced jaundice may, of course, result from the impaction of a calculus in the common duct, but jaundice may also occur in cholelithiasis (conf. p. 100) apart from such occlusion of the common duct, and it appears to me that we are justified in assuming that it may arise, without any mechanical impediment to the bile stream, as the result of infective cholangitis. (Conf. p. 80, p. 110 *et seq.*, and Case XVIII., p. 123.)

Kraus and Gans frequently found sugar in the urine during the paroxysms. (See later: Cholelithiasis and Diabetes.)

I have not often seen increased excretion of indican in gall-stone colic. In one instance it was observed in a case of typhoid fever in the second week, and also in a case which was complicated with cholecystitis and signs of peritonitis. The presence of bile pigment has been discussed under the head of jaundice. Alison frequently found peptone, and Lorenz acetone, in the urine during gall-stone attacks.

7. The spleen is, as a rule, not enlarged even to percussion (even when jaundice occurs, as I must add, in opposition to Mackay). In exceptional cases, however, one sees a conspicuous enlargement of the spleen develop rapidly, so that the organ reaches to a hand's breadth below the costal border. The cases in which I have seen this (ten in number) were all very severe, and in some instances (Case No. IV.) were complicated with biliary fever, so that they probably were examples of infective splenic enlargement.

8. The diagnostic importance of hepatic enlargement and palpable gall bladder is obvious, and needs no further discussion. Neither of these is by any means a constant symptom of the colic, and indeed the gall bladder is palpable in scarcely a third of the cases, whereas enlargement of the liver is doubtless seldom entirely absent if the examination be made during, or shortly after, the attack. Charcot was the first to call attention to this.

If the liver is swollen as the result of the attack (*i.e.*, recently) the organ is always more or less tender, and often very acutely so ; but frequently it is tender without being swollen. In such cases it is found that pain is induced when, during a deep inspiration, pressure is made with the hand as far upwards as possible beneath the right costal border. At the moment when the liver impinges upon the tips of the fingers the patient experiences a deep-seated pain which sometimes radiates over the entire hepatic region and on to the epigastrium. By no means rarely, however, the tenderness of the liver is only manifested by tension of the muscles of the anterior abdominal wall on the right side, and in such cases the difference in tension of the right and left side respectively is best observed in the rectus abdominis.

The enlargement of the liver is in some cases very considerable; for example, I have seen a previously normal liver (examined by myself) so increase in size in the course of a few days as to extend as far as the hypogastrium as a quite massive tumour, and this not by any means only in cases with severe colic, but even in those with slight pain and hardly perceptible jaundice. Under such circumstances the enlargement cannot be regarded as exclusively the result of biliary obstruction, but is probably rather due to an infective cholangitis.

The recession of the hepatic enlargement should be complete, except when an abscess, carcinoma, or diffuse hepatitis is present; nevertheless it takes place somewhat slowly (*i.e.*, only in the course of weeks) if the enlargement is considerable.

Enlargement of the gall bladder can only be recognised with certainty by palpation, and the acute enlargement which is met with in gall-stone attacks cannot always be easily detected by such means.

Sometimes the swollen gall bladder manifests itself as a highly resistant, easily palpable, and distinctly fluctuating tumour. Sometimes it can only be felt on very careful examination, and is indistinct to the touch, remains soft (Riedel's soft gall bladder), and avoids the palpating finger. It lies beneath the rectus abdominis, usually at its outer border, or even to the outer side of the nipple line. It distinctly moves downwards on deep inspiration, and upwards on expiration. Dulness is only obtained over the tumour on light percussion. The gall bladder when palpable is almost always sensitive to pressure, and is often extremely painful.

Gall-bladder tumours are not more common in cases with jaundice than in those without. Quite commonly the swelling is not continuously recognisable, disappearing one day and being again in evidence on the next. In cases in which the gall bladder is always equally and distinctly palpable it will often be found that the tumour persists after the attack is at an end, and that one has to do with cholecystitis.

In explanation of the cases in which gall bladder is swollen apart from jaundice, the existence of a valvular obstruction of the cystic duct or neck of the gall bladder due to the stone has been suggested, so that bile can enter the bladder, but cannot get out again; but the gall bladder may be distended so

as to become a palpable tumour in the course of a few days, even when the cystic duct is completely obstructed, by increase of the inflammatory secretion of its mucous membrane. Such an acute cholecystitis appears to be quite a common accompaniment of gall-stone attacks. (See Cholecystitis.)

9. Constipation is the rule, and the patients often experience, especially in slight attacks, sensations of tension and fulness of the abdomen. The character of the stools has been referred to under jaundice. The abdomen shows, in some cases, considerable distension, but this I have only observed in cases in which, apart from the attack, a tendency to tympanites exists. As a rule the abdomen is not markedly distended, but rather somewhat retracted owing to contraction of the muscles. It is not as a rule sensitive to pressure, except in the region of the gall bladder.

10. A few additional symptoms, of a general character, have still to be mentioned. The patients naturally lose all desire for food during the severe colic attacks, but even when the attacks cause but little suffering, and during the intervals between them, dyspepsia is very often, and disagreeable anorexia not unfrequently, present. Distressing headaches sometimes accompany the dyspepsia. Thirst is very common, especially during acute attacks, with vomiting and profuse sweating ; nor are sleeplessness and various nervous troubles wanting in protracted attacks.

11. *The passage of the concretions.*—In regular cholelithiasis, with which we are here dealing, the stones are passed in the motions (except in rare cases in which they are vomited). They are often sought for in vain, but such failures are usually due to the examination of the stools being not carried out continuously or over a long enough period.

This view receives important support from the fact that in private practice, in which the interest taken by the patient himself is greater, the yield is usually richer than in hospitals. The stones are best sought for by agitating the stools with water, and then allowing a sediment to fall, and repeating the process until the sediment has been thoroughly examined; or by washing the excreta through a hair sieve by means of a stream of water. The chief point is that no motion be missed, and that the systematic examination be long enough continued, *i.e.*, up to a week or longer, after the cessation of the colic.

6

As a matter of fact, it is frequently not possible to confirm the diagnosis by the discovery of calculi. I know of two cases in my own experience in which it was stated that calculi were regularly and vainly sought for during 8 years, and then, at last, concretions were found. Both cases occurred under conditions in which every guarantee of the careful carrying out of the examinations was apparently afforded. One was the case of the wife of a medical man. It is of importance in practice to learn what may be the reasons of such failures, and even when the examinations are actually carried out in such a way that stones could not possibly be overlooked, there are several possible explanations of their non-appearance in the stools.

1. The stone after having been driven into the neck of the gall bladder may have fallen back into the bladder. Charcot states that he has found this in a case which came to a post-mortem examination (as to the correctness of this view see p. 89). This can hardly be a common event.

2. The stone may have remained fixed, whereas the patency of the duct has been restored. Of this event, which is probably not very rare, we shall again speak in connection with irregular cholelithiasis.

3. The concretion may have disintegrated in the bowel. This is certainly no uncommon occurrence, as the following experiments show :—

I have made three experiments, in all cases upon healthy persons, to whom gall-stones were administered together with a teaspoonful of powdered carbon. In each instance the subject swallowed from five to seven calculi of different kinds, of about the size of peas, and all the motions were then examined until the fæces no longer showed any trace of black colour, a period which varied in the different cases. On the day following the administration of the stones an effectual aperient was given. The examination of the fæces was carried out under the supervision of a reliable medical man, in such a way that the whole of the excreta were carefully and gently washed through a hair sieve.

Only three stones of the size of peas appeared in the fæces, and these had hard and rather thick crusts of pure cholesterin. Even one stone of this kind was not recovered. Of the remaining fifteen stones, some of which were of the pure and some

of the mixed bilirubin-calcium variety, whilst others were laminated gall-bladder calculi without such a hard crust, not a single one was recovered. This is in accordance with the observation that calculi found in the motions are almost without exception hard or hard crusted cholesterin calculi belonging to groups 1, 2, and 3.

At any rate I possess only one single bilirubin-calcium stone recovered from a motion, whereas I have very many cholesterin stones so obtained, and even this specimen shows obvious signs of commencing disintegration.

The severity of the pains is not dependent upon the size of the calculus. Doubtless large stones, especially if they give rise to colic, are not as a rule passed without acute pains ; but on the other hand I have frequently seen most intense colic end with the passage of a calculus of the size of a pea. I have in my possession two stones from the same patient, both about as large as a hazel-nut, and both of about the same shape, the larger weighing 0·7 gramme, the other 0·5 gramme. The smaller of these was passed after acute colic pains, the other with less severe colic. It should, however, be mentioned that the latter was passed at Carlsbad.

As a rule the passage of the stone is easier in relapsing cases, and as has been already mentioned, in most cases of painless expulsion of calculi this result is due to the morbid dilatation of the bile passages by concretions previously passed. The stones may be found in the stools as early as 24—36 hours after the attack, but they frequently only appear after an interval of several days, and in one case in my wards they were only found 8 days after the attack.

Frequently only a single stone is passed after acute colic attacks spread over several days, and it is by no means necessary that it should be a large one. In other cases the calculi appear in large numbers in the motions, either simultaneously or in rapid succession. For example, one of my patients, after many attacks of colic distributed over 2 years, in which the stools were always examined in vain, expelled 12 hours after an attack thirty-three calculi, all of which were facetted and larger than cherry-stones. A gentleman passed in the course of 5 days, after severe colic, 244 calculi, only slightly facetted, varying from the size of a pea to that of a large cherry-stone. Another patient expelled in

four motions four, thirty-two, forty-nine, and fifteen facetted stones respectively, from the size of a cherry-stone to that of a millet-seed. Calculi which are simultaneously passed are almost always of the same kind, and usually closely resemble each other in their external features.

It is certain that all gall-stones which are passed *per anum* have not been expelled in the normal manner, *i.e.*, by the bile passages. A large number of cases are on record in which stones as large as a hen's egg, or even larger, have been expelled from the bowel. (See below Intestinal Obstruction from Gall-stones.) A stone of Blackburn's measured 9 by 4 centimeters and weighed 52 grammes. That stones of such a size should have traversed the bile ducts is out of the question, and they must have entered the intestine through a fistulous opening. In such cases definite colic has sometimes been wanting, and indeed any symptoms pointing to the presence of a calculus, previous to its appearance, so that an early author, Fiedler, whom Cruveilhier (Atlas, Livraison 12) quotes, long ago enunciated the paradox that large gall-stones give rise in their passage to less disturbance than smaller ones.

Very different views are expressed as to the maximum size of stones which are capable of passing through the gall passages, apart from fistulous openings. Courvoisier, certainly an eminent authority to whose opinion the greatest weight must be attached, has quite recently adopted the view that large calculi (as big as a nut, or even larger) pass *per vias naturales*. On the other hand, Fiedler (of Dresden) has contended that stones larger than a pea can only pass through a fistulous opening.

The common and cystic ducts are often so much dilated in chronic cholelithiasis that a full-sized finger can be introduced into them. Through ducts of such calibre large stones might pass, but the diameter of the duodenal orifice of the common duct is, even in cases with such general dilatation, always small, and according to Fiedler and Roth never more than 20 millimeters. Nevertheless it seems to me that we are quite justified in assuming that the duodenal portion of the duct is capable of considerable dilatation when a culculus passes it. It is true that in the cadaver the walls of the bile passages appear to be but slightly expansible, and in my experiments I found that even stones as large as a pea met with an almost insuperable

resistance at the *portio duodenalis*, but this affords no clue to what happens in life, for in life the walls of the bile passages appear to be much more expansible (conf. p. 61). I consider it very probable, from what I have observed in the bile passages of a living dog, that in living human beings ducts of normal calibre, and even the normal duodenal orifice of the common duct, may be traversed by stones even as large as a hazel-nut. Nevertheless the cases of Metzker, Legros, Barth, Habershon, William, and others, in which quite large calculi appeared to have been passed, apart from fistula formation, are open to criticism. In these cases there were found post-mortem large calculi which had just been expelled, or which were still enclosed in the dilated duodenal orifice, and, according to the statements, there was neither ulceration nor perforation of the ducts. The correctness of this last statement is, however, rendered very doubtful by the observations of Roth, which show that it is very easy to mistake a fistula between the common duct and the duodenum for a dilated duodenal orifice. In none of the cases referred to can the possibility be excluded that such a fistula was present, and was mistaken for a dilatation of the *osteum duodenale ductus choledochi*.

I would go so far as to believe that stones up to the size of a hazel-nut can pass *per vias naturales*, and that larger ones than this cannot do so. This is in accordance with clinical experience, for the stones which one sees passed within a few days after the termination of typical attacks of colic are not as a rule larger than a big pea, and yet gall-stones of all sizes up to that of a hazel-nut are so frequently met with that their passage must be reckoned among the regular events. The largest stone that I have seen passed after regular attacks of colic was as large and as narrow as a date-stone. I have never seen calculi which were much larger than the kernel of a hazel-nut passed after regular attacks.

We must not omit to speak here of biliary sand. Many authors speak of the passage of such sand in the stools as an often observed and established fact. It is said to appear occasionally in large quantities, even handfuls, in the motions. In order to convince me of this a colleague in Carlsbad placed at my disposal quite a collection of such biliary sand from the stools of seven different individuals. The " sand " was in each instance

of a pale yellow colour and fairly heavy, so that in washing the motions it settled quickly to the bottom of the vessel.

It consisted of small granules, from the most minute size to that of a pin's head. The granules were very hard. Yet chemical examination discovered no cholesterin and no bile pigment, or mere traces thereof; whilst under the microscope it was easily seen that one was dealing with wood cells which were often collected into masses showing a resemblance to crystalline structure. They are derived from fruits, and occur abundantly in the flesh of peas. It is true that, as has been already described, small cholesterin stones, which might be evacuated as a sand-like material, occur in the gall bladder, but such particles are as a rule too soft to survive the passage along the bowel. Harder cholesterin sand is very rarely met with in the gall bladder, but its individual particles are always clearly recognisable as such. Small bilirubin-calcium calculi in the intrahepatic duct sometimes constitute an almost black sand, and, though usually soft, they are occasionally hard; yet I have not learned that they have ever been recognised with certainty in the stools, and one should obviously only regard as biliary sand, without further proof, such evacuated material as has obviously the appearance of gall-stones, or which can be recognised to be such by chemical examination. For this latter purpose the suspected material should be washed with water, dried, and extracted with ether containing alcohol, in which cholesterin dissolves, and on slow evaporation in the air upon a watch-glass separates out in glistening crystals. The brown bilirubin-calcium stones do not, however, contain any cholessterin, and when these are in question the specimens must be examined for bilirubin. This is most simply accomplished by again carefully washing and then treating them in the cold with dilute caustic potash. If the particles consist of bilirubin-calcium a yellow solution is obtained. This solution should not be too dilute, but should have a saturated yellow tint, under which circumstances the presence in it of bile pigment can be readily recognised by means of Gmelin's reaction (with fuming nitric acid). It need only be borne in mind that many concretions consist chiefly of bilihumin, and when this is the case the green ring is not obtained by the action of nitric acid upon the potash solution, but the blue colour is clearly produced and

suffices to guard against any deception. The only possible source of error in this process is the occurrence of small lumps of altered blood, which also dissolve with a yellow colour in dilute caustic potash solution ; but the solution does not yield Gmelin's reaction, and the nitric acid tends to precipitate the albumen from it.

4. *The Course of Regular Cholelithiasis.*

The course of regular cholelithiasis varies greatly according to the severity of the individual attacks, and according as they are more or less typical or assume an incomplete or protracted character.

The disease usually first manifests itself by typical attacks of biliary colic. Fever, rigors, and vomiting are seldom wanting, jaundice may develop sooner or later, but pain is the predominant symptom. With it the other phenomena go hand in hand. The severity of the vomiting, the vaso-motor and other reflex disturbances, the possible collapse, and the whole demeanour of the patient are all dependent upon its intensity. When once the pains definitely cease the attack is at an end. Even the jaundice and enlargement of the liver then rapidly disappear. If this is not so, one must be on one's guard, since there will be stones still remaining to be passed, and fresh attacks may be expected.

A single attack seldom suffices to end the trouble, but cases are sufficiently numerous in which a single attack, scarcely lasting an hour, occurs as a transitory event; then, perhaps some months or years later, it is followed by another, or by several occurring in the same way, and afterwards the disease gives no further signs.

In most instances the disease is more severe, in so far at least as each individual gall-stone attack is made up of a series of separate attacks of colic, so that it extends over several days or even weeks. During this entire period the patient is as a rule never free from discomfort.

Such gall-stone attacks, consisting of a series of colics, may either be repeated annually at a certain season (usually it would seem in the autumn) for several years, or may occur once or twice at quite irregular intervals and then cease, the chole-lithiasis having reached its normal and favourable termination.

Departures from such normal courses are common. In the first place, the disease may assume a character entirely different from that above described, either from incompleteness of the attacks or from the absence of the cardinal symptom, namely, pain.

Cholelithiasis, presenting the features of a pseudo-intermittent fever, has been already described (p. 74). Much less obvious are the cases which I have several times met with, in which the attacks merely reveal themselves by a transitory and sometimes very considerable enlargement of the liver, not associated with any colic, but merely with tenderness of the organ on pressure, and a spontaneous, ill-defined, and disagreeable feeling of constriction in the hepatic region. I have never seen the jaundice intense in such cases, and it is usually scarcely perceptible, or absent. Among numerous cases of this kind I have seen one, at any rate, for which no other explanation was possible.

CASE V.—The patient was a nervous individual, 30 years of age, absolutely temperate and not syphilitic. All organs were normal. He often had slight pains in the hepatic region which caused him uneasiness, but by no means amounted to colic, and occasionally a slight yellowish tint of the skin. One day when, as was his wont, he presented himself for examination, although without any special complaint, the liver was found to reach below the umbilicus, was easily palpable, but showed no abnormal consistence. Its surface was smooth, and it was somewhat sensitive to pressure. The spleen was not enlarged; there was quite insignificant and indistinct jaundice. A week later the swelling of the liver had completely disappeared. Shortly afterwards a similar and equally transitory enlargement occurred. The patient went to Carlsbad, returned with his liver in a normal condition, and has since (6 months) remained free from such attacks. Gall-stones were not sought for.

There can also be no doubt that jaundice may be the sole symptom of the passage of a concretion. When such incomplete attacks are met with in cases of cholelithiasis, typical attacks of colic almost invariably replace them at intervals. In the enormous majority of cases the outcome is favourable; after a series of attacks no more occur, and the matter is at an end, leaving behind it, as a rule, no impairment of health; occasionally, however, relapses occur years afterwards.

On the other hand, the disease may have an unfavourable ending by the occurrence of sudden death during the attack, or

by the development of irregular cholelithiasis. As causes of sudden death during the attack of colic, suicide, to which the patient is driven by the pain, and cerebral hæmorrhage have been mentioned, but I have not found any unquestionable cases of such accidents. On the other hand, there are cases which prove fatal during the attack, apparently from pain or shock, in which post-mortem no complication can be discovered. For example, Gerhardt records the case of a man who died during the attack from reflex spasm. A patient of Kraus's, with fatty heart, collapsed suddenly after the attack. Leigh lost a patient from collapse after an attack of colic lasting 16 hours. In the older literature, too, there are cases of this kind fully described by Chomel, Briquet, Champaignac, Delaunay, Lieutaud (quoted by Fauconneau-Dufresne), and also by Portal. Gerhardt found the calculus in the cystic duct. In Leigh's case, to which Charcot refers, a stone lay in the gall bladder, and Charcot held, with Leigh, that it had slipped back into this situation. However, Leigh did not search the bowel, and it is very possible that, as in Kraus's case, a second stone had already made its way into the intestine. In a few instances the stone has been found impacted in the common duct; in Kraus's it had already passed into the duodenum. Moreover, in quite exceptional cases the attack has a fatal ending by producing perforation of the gall bladder or large bile ducts. In Courvoisier's work I find forty-one cases collected which were certainly of this kind, in thirty-three of which the gall bladder, in six the common duct, and in two the cystic duct were perforated. In all the cases the fatal ending was due to the escape of bile into the abdominal cavity, followed by peritonitis. This result is only to be expected. Pure bile does not necessarily set up peritonitis, as is shown in cases of injury to the normal biliary passages with escape of bile into the peritoneum, but in these cases of cholelithiasis the bile is, usually at any rate, no longer pure, but infective.

In 1881 I had experience of a case in Königsberg which showed that by timely surgical interference the fatal result of such peritonitis from perforation in cases of gall-stone colic may be averted.

CASE VI.—A woman, aged 50, had suffered for some months from severe attacks of typical biliary colic, accompanied by jaundice. No

calculi were found. In the course of an attack the colic pains ceased suddenly, and severe collapse set in. A few hours later there followed most acute pains, now diffused over the abdomen, with severe vomiting, abdominal distension, and rapidly increasing exudation of free fluid into the peritoneal cavity. On the third day from this Professor Schoenborn performed laparotomy at my instigation. By means of an incision about 10 centimeters in length in the middle line between the navel and symphysis an abundance of slightly bile-stained seropurulent fluid was evacuated from the abdominal cavity. The cavity was drained, and the patient made a most satisfactory recovery, uninterrupted by any untoward event. Eight years afterwards the patient was alive and in perfect health. No signs of cholelithiasis had ever reappeared.

This appears to be up to now the only case of the kind successfully operated upon.

5. *Diagnosis of Gall-stone Attacks.*

The diagnosis of gall-stone colic is, as a rule, easily made, even from the description which the patient gives of the attack. The severity of the pains, their situation in the hepatic region, the rigors and jaundice, are of special importance. Even when pain is the sole manifestation of the attack its nature can be correctly inferred, at any rate if it has already frequently recurred. In such cases the commencement of the attack about midnight is an important feature. This point, taken together with the situation of the pain, is of special importance, when a confusion with cardialgia, and still more with gastric ulcer, has to be excluded. In gastric ulcer the pains usually commence suddenly a few hours after a meal, but they sometimes attain their maximum severity in the early part of the night.

With gall-stones the pains are occasionally to some extent dependent upon the taking of food, and during the days in which the concretions are on the move, the uncomfortable sensations from which the patient continuously suffers are increased when food is taken. Moreover, the actual attacks of severe pain are, as has been already mentioned, often started by errors of diet, although they commence many hours after the meal that excites them. The gastric digestion is often quite undisturbed in cholelithiasis, so that the patient can digest anything as soon as the attack has passed off. Severe retching and bilious vomiting is a very characteristic feature of gall-

stone colic, but these occasionally occur in cases of gastric ulcer also. Jaundice is of course the safest sign of all, and its dependence upon gall-stones is often revealed by its rapid appearance and increase after a colic attack, or perhaps dyspepsia, and by its fading away equally rapidly in the course of a few days. The so-called catarrhal and epidemic jaundice almost always persist for weeks. When separate attacks of jaundice with intervals of definite immunity (marked, for example, by the complete disappearance of the yellow tint) are met with, we practically always have to do with gall-stones, at any rate in our part of the world, as (according to Courvoisier) Baglavi recognised, and as Murchison very distinctly stated. In the absence of jaundice it may be no easy matter to distinguish gall-stone colic, not only from cardialgia, lead colic, renal colic, and constipation with intestinal colic, but also from peritonitis, and especially perityphlitis, and even from intussusception. For the diagnosis of lead colic the presence of lead poisoning, shown by the lead line, is conclusive. Sufferers from lead poisoning are almost always males, whereas those with gall-stones are in the great majority of instances females. In other respects the resemblance may be a very close one, but in lead colic the liver is not enlarged or tender on pressure. In renal colic the pain has, in my experience, always had its seat in the lumbar region, and this I have never seen in gallstone colic. Intestinal colic with coprostasis often causes severe pains, and these are sometimes confined to the right hypochondrium. The immediate relief afforded by relief of the bowels, and even by the passage of flatus, are characteristic of this condition, and in coprostasis the pains never attain to the severity of those of gall-stone colic.

I have found the diagnosis between gall-stone colic and peritonitis by no means easy in a number of cases. In both there may be great collapse. Tenderness on pressure and distension of the abdomen may be conspicuously absent in peritonitis, and are of little service for the distinguishing of the two disorders. The same is true of the pulse which may be very rapid in gall-stone colic, and may be very slow at the commencement of peritonitis. Difficulty in micturition is not very uncommon in gall-stone colic, especially when morphia is employed. Confusion with general peritonitis is best avoided

by observing the type of breathing. In diffuse peritonitis the diaphragm is quite motionless, and consequently the respiration is purely costal. I have only once seen this in gall-stone colic, in a case with cholecystitis, in which there was undoubtedly severe peritonitic irritation. In cases which are under observation for some time the character of the fever is important, for in peritonitis this is not intermittent, at any rate not from the outset.

Perityphlitis may assume a very close resemblance to gall-stone colic. In this condition the pains may have a distinctly colicky character and may be very severe. Usually, of course, their seat is in the right hypogastrium, and resistance is there felt. Nevertheless the pain and resistance may have their seat in the right hypochondrium just below the costal border. This is not surprising, seeing that the vermiform appendix is not infrequently displaced upwards, so that, together with the ascending colon, it rises as high as the liver. In one case, for example, a perityphlitic abscess actually lay in contact with the sharp edge of the liver, and in another instance I found the vermiform appendix adherent to the gall bladder. In practice it is very important to bear this in mind, for it is better that the diagnosis should remain in doubt for a time, than that harm should be done by unsuitable interference, if the case be one of perityphlitis.

In such case, the examination of the urine for indican is not without value. I have never failed to find excess of indican in recent cases of typhlitis in which I have examined for it, but in gall-stone colic I have hitherto only met with such excess in exceptional cases.

Moreover, in my experience these difficulties of diagnosis only arise in the slighter cases of gall-stone colic. In such cases it is usually possible to relieve the pains by narcotics, at least temporarily, and by such means complete relief is usually obtained, whereas in typhlitis such complete relief is not easily brought about.

The enlargement of the liver and the tenderness on palpation when present do not usually disappear under some days or even weeks. This is, in default of jaundice, the only sign which outlasts the attack, and consequently is a sign of great value, as Charcot was the first to insist.

Those gall-stone attacks, which are almost painless, are sometimes only suspected on account of such transitory enlargement of the liver. If the enlargement is considerable, and the recession only gradual, and if there be an associated enlargement of the spleen, the exclusion of cirrhosis may present some difficulty.

In the older works, and even in that of Frerichs, cases of hepatic neuralgia are recorded which, according to the descriptions, presented a very close resemblance to gall-stone colic. I regard the occurrence of such hepatic neuralgia in association, be it understood, with enlargement of the liver and jaundice as not proven.

It appears to me that we are not in a position to attempt to determine definitely the spot in the biliary passages in which a stone is impacted. In cases with severe jaundice it is usually lodged in the common duct. Yet this is not always so. (Conf. Chronic Jaundice from Gall-stones.)

B. IRREGULAR CHOLELITHIASIS.

1. *Incarceration of Calculi.*

Various morbid affections of the biliary passages and liver can develop as sequelæ of cholelithiasis; such, for example, as infective cholangitis, cholecystitis and hepatitis; ulcerations; pericholangitic and pericholecystitic inflammations, and the formation of fistulæ, new growths in the bile passages, and diffuse hepatitis.

The development of these sequelæ is for the most part brought about by the permanent incarceration of concretions. The concretions may become incarcerated in any part of the system of bile ducts, that is to say, be held so fast that their further progress, without violence to the enclosing duct-walls, is rendered impossible.

The incarcerated stone lies, or the incarcerated stones lie, either in recesses opening out from the side of the duct or in the lumen of duct itself, and of these alternatives the latter is the commoner. Under such circumstances the lumen is usually entirely obliterated, either in front or behind, or on both sides of the stone, or at any rate is so narrowed that only an

extremely fine probe can be passed along it. By no means unfrequently, however, the stones lie either singly or several together in a dilated bile duct, so that the bile still finds a passage alongside of them. When the calculus lies in a closed cavity it may either be closely enveloped by its walls, or these may allow it a certain amount of play. The surface of the calculus may be embraced by the walls, in which case it bears the impression of their inner surface, or may be adherent; or, on the other hand, it may be embedded in a soft mass of cholesterin crystals and epithelium, or even in actual pus.

The stones may be found incarcerated in a recess of the gall bladder which corresponds to the fundus, whilst the gall bladder itself may show a natural appearance, and be filled in a normal manner with bile. More frequently the stone is firmly fixed in the neck of the bladder, under which circumstances the gall bladder is usually shrunken, but it may be dilated.

Calculi are by no means unfrequently found in the cystic and common ducts. Schloth (of Erlangen) found them in the cystic duct in 4·6 per cent., in the common duct in 2·6 per cent., of all autopsies on patients with gall-stones. At Basle Courvoisier found 6·7 per cent. and 3·9 per cent. The highest figures for such occurrences are those of Schröder (in Strasburg). He found calculi in the cystic duct in 13 per cent., and in the common duct in an equal proportion of 141 autopsies on patients with gall-stones. Here again the result may be due to the fact that Schröder's statistics include a larger proportion of elderly persons.

In by far the greater number of cases stones found in the cystic and common ducts have become incarcerated, and are not merely on their passage along the ducts. This is proved by their size, as is seen from the following table of Courvoisier's:—

CALCULI IN CYSTIC DUCT.

Of the size of a pea or bean	18
As large as a hazel-nut or cherry, or of the diameter of a finger	26
As large as an almond or nutmeg	4
As large as a walnut...	6
As large as a plum	1
Large, bulky	8
	63

CALCULI IN THE COMMON DUCT.

Sand or gravel	2
As large as a pea	15
As large as a bean or cherry-stone	6
As large as a hazel-nut or cherry	30
Of the diameter of a finger	5
Somewhat larger than this	9
As large as a walnut or pigeon's egg	16
As large as a hen's egg or plum	3
Larger than these	8
Large or very large	18
	112

It will be seen from this that among sixty-two calculi in the cystic duct there were forty-four, and among 112 in the common duct there were eighty-five which attained to or exceeded the size of a cherry. As a rule there is a single calculus of the size of a cherry or larger, which lies fixed in the duct and embraced by the mucous membrane, or several such of greater or lesser size may be packed together into a group. Where the calculi are of the size of a pea or smaller there is usually a larger stone also present, which lies to the duodenal side of the others and has become incarcerated. In the common duct the calculi usually lie at the duodenal end. On this point also I reproduce Courvoisier's tabulated statistics. Among 123 stones there lay—

At the commencement of the duct	17
In the middle of the duct	19
Near the duodenum	20
At the osteum or papilla	41
The entire duct was blocked in	26 cases.
	123

Calculi are very rarely met with in the hepatic duct (Schloth in 0·3 per cent., Courvoisier (Basle) 1·3 per cent., Schröder (Strasburg) 1·4 per cent.). In such instances also the stones are of the size of a cherry or larger, and are incarcerated in the main duct or in one of its principal branches. In the liver itself stones of larger size are very rarely met with ; but, on the other hand, small concretions of bilirubin-calcium are quite common in the intrahepatic ducts. Schröder found them in 9 per cent. of cases with gall-stones, but they are actually much more common than this, for such biliary gravel is often present

in the ducts in the liver, in cases in which no actual gall-stones are present. These tiny formations may lie singly in the bile, by which they are easily washed away, or may be collected into masses in one or many of the intrahepatic ducts, so as to fill them. Tubular bilirubin concretions, hollow casts of the bile passages, are not very rare in the smallest hepatic branches even in human subjects, as has been mentioned in several places in this work. Similar casts of the larger branches are somewhat frequently met with in oxen, but in human beings they are extremely rare (conf. Courvoisier, p. 37). Cruveilhier, Frerichs, Courvoisier, and others have recorded cases in which the entire system of bile ducts from the *papilla vateri* to the smallest intrahepatic branches were found completely packed with stones of various sizes.

Of the stones which are to be found in the bile ducts, those in the smaller branches of the hepatic duct have been formed *in situ*, but those in the large extrahepatic duct have usually been carried thither. The great majority of them come from the gall bladder, and accordingly one often finds, in addition to the stone in the common or cystic duct, or even in the main trunk of the hepatic duct, concretions of an exactly similar nature remaining in the bladder. Emerging from the gall bladder, the calculi enter the cystic, and thence pass into the common duct, but they can also without difficulty pass into the trunk or principal branches of the hepaticus, since after they have passed along the cysticus and have reached the entrance of the common duct they can easily be pushed in the direction of the liver by after-coming calculi or bile, if their passage into the common duct is rendered too difficult by resistance, as, for example, when the duct is already filled with calculi. On the other hand, concretions in the hepatic and common ducts may also have had their origin in the intrahepatic bile passages; at any rate we must assume this to have been the case when these passages are found packed with concretions. (Compare the drawing in Cruveilhier's Atlas, Livraison 12.)

If the concretions lie for some time in the larger duct they probably undergo further growth there. On p. 35 it was inferred that the materials necessary for this purpose, viz., lime and cholesterin, are yielded by the mucous membrane of the principal bile passages, as well as by that of the gall bladder.

Many calculi obtained from the principal ducts show clearly by their structure both that they have originated in other situations and that they have undergone a further increase of size in their ultimate resting-place.   Their form, cylindrical, oval, or even spherical, corresponds to the lumen of the bile duct in which they are found, whilst on section one finds in the centre a sharply defined nucleus, the layers of which, if any are present, are in no way parallel to the inner surface of the cavity in which the calculus is situated.   The crust, on the other hand, shows laminæ which are parallel to the surface of the concretion or, in other words, to the inner surface of the mucous membrane which encloses it.   In rare cases, however, the concretions are not immigrants, but have been actually formed in the ducts themselves.   This is obviously true of hollow casts, which can be produced *in situ* in the bile ducts.   Under such circumstances there is no extraneous nucleus.   On the other hand, a foreign body may serve as a nucleus, as in the case described by Lobstein, in which a round worm served as such.

Under any circumstances it is unusual for gall-stones to originate in the (extrahepatic) bile ducts, whilst their growth in the ducts at the spot at which they are impacted appears to be a regular and very important process.   In this way alone can the frequent occurrence of large stones in the biliary passages be explained, and the majority of stones which are found in such situations are larger than a cherry.   It is improbable that calculi of such magnitude, not to speak of those which attain the size of a plum or even of a hen's egg, move along the ducts (conf. p. 85).   The large stones which are thus met with were smaller when they entered into the place where they are found, and have only attained their final dimensions *in situ*.

The same is true of the large calculi, of the size of a walnut or even larger, which make their way out of the common duct through choledocho-duodenal fistulæ (conf. p. 85 *et seq.*).   These have lain fixed for a time in the common duct behind its duodenal portion, and have only reached their actual dimensions during their sojourn in that situation.

It appears to me very probable that the growth of calculi may progress quite as rapidly in the common duct as in the gall bladder.   The occlusion of the duct by the calculi is not at first

7

complete, and for a time a stream of bile, intermittent it may be, flows past them. From the bile which bathes the calculi a rapid deposition of bilirubin-calcium may take place upon their surfaces. It is true that no absolute proof that this occurs is forthcoming, but the fact appears to be established by the following case :—

CASE VIII.—Woman, aged 60. The patient has suffered in the winter of 1888–89 from numerous gall-stone attacks, and afterwards remained well until the winter of 1889–90, when a few less severe attacks occurred.

On May 30th, 1890, the patient experienced, after a meal, acute pains in the abdomen, especially on the right side, together with a rigor and afterwards profuse sweating. Since then the pains have persisted without material amelioration. Up to June 2nd the patient had several attacks of vomiting daily, but nothing beyond small quantities of
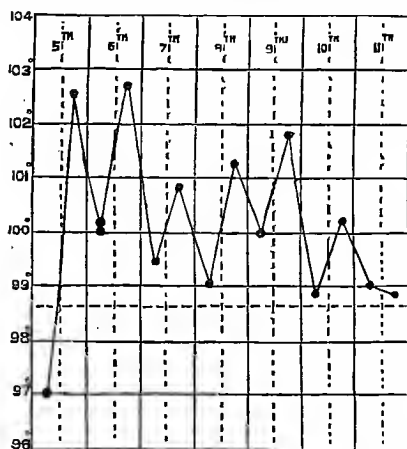
mucus was ever brought up. She states that the urine has been black from the commencement of the attack. There is jaundice of the skin and sclerotics.

June 6th : In the right mesogastrium, between the nipple and parasternal lines, a tumour is felt of the size of a hen's egg, extending laterally beyond the nipple line. This tumour is moderately tense, smooth on the surface, fluctuates distinctly, is depressed by inspiration. The tumour cannot be traced upwards to the border of the liver, from which it is separated by a furrow. The liver is not clearly palpable. Pressure over the entire hepatic region causes pain. The liver dulness extends for 2 inches below the costal border, and the tumour is dull on percussion. The abdomen is distended; the urine contains a large amount of bile pigment. Pulse 80. Temperature: morning 38°, evening 39·2°. Treatment: poultices, Carlsbad water taken hot.

June 7th : Pains abating.

June 8th : The pains have ceased, and the tumour has disappeared. A stone was found in a motion of about the size and shape of a date-stone.

July 17th : Patient discharged, cured.

The stone which was passed showed a roughly cylindrical shape, with both ends blunt and rounded. It consisted of a brittle shell of bilirubin-calcium, 2—3 millimeters in thickness, and within this lay a somewhat elongated nucleus resembling a gall-bladder calculus. It possessed a somewhat firm crust of bilirubin-calcium and cholesterin, 2—3 millimeters in thickness, and had in its centre a cavity, which contained a crumbled mass of cholesterin (the calculus was examined in the dry state).

The assumption seemed to me to be justified that in this instance, on May 30th, at the commencement of the last colic attack, a stone from the bladder had made its way into the common duct, and had remained there until its expulsion, not later than on the 7th or 8th of June, and that during this period of 8 days the outer shell of bilirubin-calcium of 2—3 millimeters in thickness had been formed.

The incarceration of gall-stones is, as has already been said, the starting-point of irregular cholelithiasis, and gives rise to the development of the numerous infective and mechanical disorders of the biliary passages, by which this condition manifests itself.

Without any complicating condition incarceration of calculi may lead to chronic jaundice, but even this may be wanting, and the condition may not only remain latent, but may even be absolutely harmless. This last is not uncommonly the case if the stones lie in the gall bladder or cystic duct, and their presence there, provided that no infective or mechanical disorder is produced, only gives rise to disturbance when the calculus is extraordinarily large. Again, the concretions frequently remain quite innocuous if they are situated in the smaller branches of the hepatic duct, for the blocking of one, or even of many such branches seems to be of no consequence in itself.

Calculi which are held fast in the main trunk of the hepaticus or in the common duct usually cause jaundice, but they do not by any means always produce this effect. There have been numerous cases in which large concretions in these

main channels have produced no jaundice, and have also failed
to produce any other ill effects.

I removed a large cholesterin calculus from the body of a
man who died of leukæmia, and who never had any symptom
of cholelithiasis—the bile flowed past the stone.   Still more
remarkable are the cases of Cruveilhier and Courvoisier, already
referred to, in which the entire system of ducts, from the
papilla to the finest branches of the hepatic duct within the
liver, were packed full of calculi ; and yet the bile had found
free exit, and all the symptoms and evil results of cholelithiasis
were wanting.

Moreover, stones which have lain latent for a long time in
the common duct may suddenly occlude it.   Three cases of this
kind have been recorded by Spencer, Paulicki, and Pepper, in
each of which a stone of the size of a walnut was found post-
mortem blocking the common duct.   The first symptoms which
could be associated with the gall-stone had come on suddenly,
simultaneously with jaundice, only 10 days before death ; and
yet the calculus, as its large size showed, had in each case lain
for a long time in the duct.

In the great majority of cases, however, even small con-
cretions lying in the trunk of the hepaticus, or in the common
duct, produce obstruction and consequent jaundice.

2. *Chronic Jaundice from Gall-stones.*

Jaundice of a chronic type, *i.e.*, lasting for months or longer,
is very common in cholelithiasis.   This may be due to incar-
ceration of stones in the bile passages, and is a natural result
of incarceration of calculi in the common or hepatic duct.   But
calculi which are fixed in the cystic duct may also cause
obstruction of the choledochus, and are, as a matter of fact,
more frequent causes of jaundice than stones in the hepaticus.
Thus, for example, Wilson found in a patient, who died after
jaundice of 4 years' duration, the common duct dilated and free
from stones, and the cystic duct much dilated (9 centimeters
long and 6 centimeters broad) and filled with calculi.   In cases
of operation for chronic jaundice this condition has frequently
disappeared rapidly, after stones had been removed from the
cystic duct alone, by cholecystotomy, &c., as, for example, in

two cases of Bardenheuer (quoted by Stauff and by Strohl), and in one case of S. Jones's.

But chronic jaundice is apparently by no means uncommon in cholelithiasis, apart from the actual presence of calculi in the ducts, for the greatly distended gall bladder may compress the common duct.   Thus Ramskill found, in the case of a man who died after severe cholelithiasis, attended by jaundice but without complete discolouration of the stools, that this was due to the distension of the gall bladder by two large calculi.   In a case of Socin's there had been severe jaundice for 5 months, and on cholecystotomy 500 stones were found in the gall bladder. At the autopsy (2 days later) the ducts were found completely free.

In the same way dropsy and empyema of the gall bladder, apart from calculi, appear to be capable of producing jaundice. Thus, in a case recorded by Kümmell, jaundice of considerable duration disappeared after the pus was evacuated from the gall bladder tumour, although no stones were found.

Musser and Keen relate the following case.   In a woman, aged 31, extreme jaundice developed after symptoms which might very well have been those of gall-stone colic, and which had lasted 6 months at the time of the examination.   There was a gall-bladder tumour extending downwards some 8 centimeters below the border of the liver, and of the same width. At the operation (cholecystotomy) about three-quarters of a litre of slightly purulent fluid was evacuated from the gall bladder, and then followed bile.   No calculus was found.   At the autopsy the cystic and common duct were found much dilated.   A little finger could be introduced into the common duct, and the ostium duodenale was so broad that it allowed a thumb to pass (choledocho-duodenal fistula).

This case without doubt presented the sequelæ of cholelithiasis, but the gall-stones had been long ago expelled through the choledochus-duodenal fistula.   There was no apparent cause for the biliary obstruction, unless we admit as such the compression of the common duct by the enlarged gall bladder. Irving operated upon a similar case.

There are, moreover, cases of an exactly similar type, save that instead of empyema or dropsy of the gall bladder there is merely excessive distension of the bladder with bile.

CASE IX.—Woman, aged 60. Was attacked 6 weeks ago with all the symptoms of gall-stone colic, and since then there has been intense jaundice. Liver enlarged and slightly tender. Gall bladder clearly felt as a small tumour of the size of an apple beneath the border of the liver.

An exploratory puncture yielded normal bile (proved to be sterile by a culture experiment). The patient died with increasing debility. Autopsy: Greatly distended gall bladder, and dilatation of the main trunks of the bile ducts. In the liver the hepatic ducts were only slightly dilated. The mucous membrane of the bile passages was normal throughout; no calculi were found. The liver was bile stained, and showed trifling fibrous tissue increase in the interlobular spaces and in the adjacent portions of the lobules.

In such cases we might suppose that there is paralysis of the gall bladder as a result of past gall-stone colic. It is unquestionable that such paralysis occurs as a result of long-standing impaction of gall-stones. Petit, Jacob, and Cyr quote cases of such paralysis of the gall bladder. That of Cyr is the most instructive. A very cachectic woman presented a tumour of the size of an orange in the region of the gall bladder, which emptied itself under the slightest pressure, and then the empty bladder could be grasped. Jaundice may develop in such cases in consequence of compression of the common or hepatic duct by the distended gall bladder, and perhaps by re-absorption of bile from the permanently over-filled bladder (?). As a rule, however, in chronic jaundice with cholelithiasis, the obstruction is situated in the common duct. Unfortunately this obstruction is not always a calculus there incarcerated, but there may exist instead of, or together with this, carcinoma, or cicatricial stricture of the bile passages, or abscess, &c., in the neighbourhood of the duct, which interferes with the outflow of bile.

Among the cases of chronic jaundice after cholelithiasis which come to post-mortem examination there are comparatively few of uncomplicated closure of the common or hepatic duct by incarcerated stones.

Hilton Fagge stated (in 1875): "When a patient who has had attacks of biliary colic dies of protracted jaundice the bile passages are almost invariably found to be affected with cancer." I regard this, indeed, as an overstatement, yet Murchison in his lectures on the diseases of the liver only

brings forward two cases of fatal uncomplicated chronic jaundice due to gall-stones, and even in 1887 Glover regarded every such case as worthy of publication on account of its rarity. Nevertheless it would be an error to infer, from the great rarity of the uncomplicated cases of this kind coming to post-portem examination, the rarity of the condition itself. Chronic jaundice due to incarceration of calculi in the choledochus is common enough, only it is not usually fatal as such. Either the obstructing calculus is in the end expelled or serious complications develop.

In the course of a by no means exhaustive review of the literature I have found nineteen sufficiently fully reported post-mortem records of cases which succumbed to simple obstruction of the common duct by gall-stones. I take this opportunity of thanking Dr. Kien for one such case, and I have seen one myself.

In seventeen cases the stone lay at the duodenal end of the duct, in two the position of the stone is not accurately described, in two others it lay at the commencement of the duct. In each of the first seventeen cases the possibility existed of cure by the formation of a choledocho-duodenal fistula. In five such a fistula had already been formed, but was still too small to allow of the passage of the stone or stones.

Choledocho-duodenal fistulæ are very common, much commoner, indeed, than has hitherto been supposed, for they have frequently (compare above Roth, p. 85) been regarded and described as dilatations of the *osteum duodendale ductus choledochi*. All such cases of fistula, however, are examples of perforation by gall-stones, and the relief of chronic jaundice due to gall-stones in this way is not an unusual event.

The chronic jaundice of cholelithiasis is at any rate dependent upon obstruction of bile, as a result of which, dilatation of the ducts is always brought about.

The common duct is usually dilated in its whole extent, but it may be narrowed or obliterated on the duodenal side, and only dilated on the hepatic side, of the stone by which it is obstructed. The dilatation may be cylindrical or globular. The common duct may be dilated into a huge sac, capable of holding a litre or even more, and may then be taken during life for a dilated gall bladder, and the same mistake may even

be made at an operation or post-mortem examination. The hepatic duct, and even its intrahepatic radicles, share in the dilatation. Frequently the dilatation of these ducts is very conspicuous.

The much dilated hepatic duct has been taken for a dilated gall bladder, opened, and stitched to the abdominal wall, at the operation of cholecystostomy. In one case which came under my own observation such a dilated duct projected below the border of the liver as a distinctly fluctuating tumour, and was naturally regarded as the gall bladder. Even at the autopsy the sac filled with bile was mistaken for this structure, and it was only after careful preparation that it became evident that we had to deal with a dilated main branch of the hepatic duct. In the liver itself the smaller bile ducts can be so greatly enlarged that the liver in its entirety, or one or other of its lobes, may resemble a sponge filled with bile. Such extreme dilatations of the biliary passages are rare, but enlargement of the common duct sufficient, for example, to allow of the introduction of a finger or thumb, or of the smaller intrahepatic duct to the size of a crow-quill, are quite frequent. These last, which are usually unequally dilated, being larger in some parts of their course than in others, often appear on the surface as cylindrical or varicose tubes filled with bile. These have before now been ruptured as the result of slight injuries.

Dilatation of the cystic duct and gall bladder is much less constant, but the cystic duct may be so greatly enlarged as to become a cyst, and the same is true of the bladder. It is, however, an important fact that the gall bladder is in the great majority of cases shrunken rather than dilated. Courvoisier was the first to observe this ; he remarked very truly that the frequent absence of distension of the gall bladder in chronic jaundice from gall-stones is of importance for the diagnosis of the condition, since in chronic biliary obstruction due to new growths of the common duct or pancreas such distension is much less frequently wanting.

The walls of the dilated ducts are often thickened. Earlier writers, such as Barth, Deville, and Broca believed that they could demonstrate hypertrophy of the muscular coat in the wall of the dilated common duct. Nevertheless there are no conclusive investigations establishing this point, but on the other

hand there is as a rule fibrous thickening of the duct-wall, associated with atrophy of the mucous membrane.

As a result of biliary obstruction a diffuse chronic inflammation may develop in the liver, which will be discussed later in a separate section.

One frequently sees chronic jaundice develop after an attack of gall-stone colic. Such an attack leads to pronounced jaundice, and the colic recurs at first frequently and afterwards at longer intervals, whilst in each attack the jaundice tends to become more intense. Matters may go on in this way for months or years. Either the pains lose their intensity, whilst rigors continue to recur in a regular manner, or all subjective symptoms may disappear, the jaundice alone persisting unaltered, and even this almost always exhibits very conspicuous variations of intensity.

The stools are seldom permanently free from bile. They often are so temporarily if the above-mentioned attacks of pain, attended with increased jaundice, occur. It is well known that paroxysmal exacerbations of all the symptoms, which cannot be distinguished from true gall-stone colic, may occur even in cases in which the stone has long lain quite fixed and immovable. These appear to be connected with transitory increase of the disturbance of the bile flow, the causes of which are to be sought in swelling of the mucous membrane enclosing the stone, in the obstruction of the passage, which still remains by the side of the stone, by thickened bile, or in other similar occurrences.

When the jaundice disappears entirely this is not always a proof that the stone has passed, *i.e.*, has forced its way through into the duodenum. As Aufrecht's case and many others show, a duodenal fistula may be formed, through which the bile flows away and the jaundice is caused to disappear, although it be too small to allow the passage of the stone, which accordingly remains *in situ*. As a rule there have been many previous attacks of colic, and it seldom happens that the actual first attack of colic leads to chronic jaundice. I may here quote a case in which this occurred:—

CASE X.—Schoolmistress, 32 years of age, hitherto quite healthy, suffered 10 weeks ago from dyspepsia for a few days, and from slight pains in the right hypochondrium. Then followed acute colicky pains,

with jaundice which quickly became intense, and white stools. The
attacks of pain recurred almost daily, being sometimes attended with
slight rigors. After taking, for 10 days, a solution of Carlsbad salts
(ordered by her medical attendant) there was a somewhat sudden remis-
sion of the pains (10 weeks after the commencement of the illness), and
2 days later bile-stained stools, in one of the first of which the gall-stone
was found. This was as large as a sparrow's egg, consisting of an old
and beautifully crystalline stone of pure cholesterin as a nucleus and
a crust of amorphous cholesterin hardly 1½ millimeters in thickness.
Since then the fæces have continued to be bile-stained, there has been
no return of pain, and the jaundice is already disappearing.

Chronic jaundice from gall-stones may also occur without
pains or any other symptom whatever pointing to gall-stones
having ever been previously noticed. Courvoisier found ten
cases of this kind recorded, and I have myself had one such
under treatment for months in Königsberg. The patient per-
sistently denied having experienced any gall-stone troubles
(even rigors). At the autopsy three calculi of the size of small
walnuts were found incarcerated in the common duct close
to the *portio duodenalis* and completely closing it. The course
of such chronic jaundice is liable to great variations. Recovery
may take place even after it has lasted a long time. In the case
above described I saw the stone spontaneously passed after 3
months, and in another undoubted case the expulsion took place
after 4 months.

CASE XI. was that of a man, aged 60, who had suffered from colic for
years. For the last 4 months intense jaundice with almost daily colic
pains, frequent rigors with elevation of temperature, great weakness,
and cachexia. Liver smooth, extending two fingers' breadth below the
costal border ; gall bladder not palpable; spleen palpable, moderately
enlarged; no ascites. At Carlsbad the expulsion of the stone occurred,
as far as could be judged by the suddenness of his improvement, but
the calculus was not found. Complete recovery.

Frerichs saw recovery, also at Carlsbad, after obstruction
of the common duct for 7 months. Osler records a cure by
passage of the stone after 9 months, and Page after 1½ year's in-
carceration, with constant jaundice. The body weight of Page's
patient fell from 267 to 140 pounds whilst the jaundice lasted.

Murchison even records a case in which, after jaundice
had persisted for nearly 4 years (according to my reckoning ;
Murchison puts it at nearly 6 years) recovery took place, the
symptoms pointing to expulsion of the stone.

In all these cases the ultimate passage of the stone may very well have followed upon the development of a choledocho-duodenal fistula. Even in that of shortest duration (the first of my two cases) the expelled stone was far too large to have been able to pass through the *portio duodenalis*.

Death may ensue after the jaundice has only lasted a short time. Cases are recorded (by Spencer and Petter) of chronic incarceration of calculi in the common duct which had a fatal ending 10 days after the development of jaundice. Handfield Jones's patient died at the end of 8 weeks, and those of Williams and of Glover at the end of 3 months. In most instances death has occurred between the sixth and twelfth months, but cases of more than a year's duration are not uncommon. Courvoisier found six recorded cases of jaundice due to gall-stones, confirmed by autopsies, which had a duration of from 2—5 years. Death almost always occurs with the symptoms of so-called cholæmia, that is to say, with the development of coma, and often, at any rate, with the development of a hæmorrhagic diathesis; rarely it is the result of perforation and peritonitis.

The diagnosis of incarceration of gall-stones as the cause of chronic jaundice often remains doubtful. The history of the case is undoubtedly very important, but cases are by no means rare in which all history characteristic of cholelithiasis is wanting; and on the other hand, in cases in which the history points to cholelithiasis there is unfortunately no mere block-age of the bile ducts by calculi, but instead of, or in addition to calculi in the common duct, there is a new growth or cica-tricial constriction.

The following indications point, as a rule, to the presence of gall-stones in the common duct as the cause of a chronic jaundice :—

1. The continuous or occasional presence of bile in the fæces.
2. Distinct variations in the intensity of the jaundice.
3. Normal size or only slight enlargement of the liver.
4. Absence of distension of the gall bladder.
5. Enlargement of the spleen.
6. Absence of ascites.
7. Presence of febrile disturbance.
8. Duration of the jaundice for more than a year.

With regard to 1 and 2. The presence of bile in the fæces in jaundice from gall-stones has been already somewhat fully discussed on p. 77. The occasional presence of bile in the motions is very important. When the common duct is obstructed by new growths or by cicatrices the fæces should be devoid of bile, and should remain so to the end.

Variations of intensity of the jaundice appear to occur in cases of new growths also, but the fluctuations are in such cases less distinct than in those due to gall stones. In the majority of cases of chronic gall-stone jaundice well-marked remissions frequently occur, which are all the more characteristic if at the same time bile reappears in the motions for weeks together. Cases of gall-stone jaundice do indeed occur in which the jaundice remains of equal intensity, and the fæces are colourless for months or years together, but they are extremely rare.

The almost complete or complete disappearance of the jaundice and the simultaneous reappearance of bile in the fæces is certainly far rarer in cases of jaundice due to new growths. I only know of one case of the kind, recorded by Coupland, in which this repeatedly occurred, and there was a simultaneous diminution in the size of a palpably dilated gall bladder. The case was one of new growth in the wall of the duodenum near the *papilla vateri*.

On the other hand, in any case of chronic jaundice it may happen that the yellow colour of the skin and sclerotics diminishes considerably, apart from any restoration of the outflow of bile into the intestine, and whilst the stools remain completely bile-free. The cause of this is an arrest of the secretion of bile in the liver, and these are the cases in which at the autopsy the dilated bile ducts are found to be no longer filled with bile, but with a faintly tinted mucous secretion.

With regard to 3. The absence of considerable enlargement of the liver is quite frequent in chronic jaundice from gall-stones. In carcinoma of the gall bladder, marked enlargement and nodular condition of the liver does not, as a rule, long remain absent. On the other hand, with obstruction of the common duct, as with carcinoma of the pancreas, the liver usually remains small.

With regard to 4. As was stated on p. 104, dilatation of the gall bladder is usually present in jaundice due to carcinoma of

the pancreas, and other new growths which compress the common duct, whereas it is often wanting in chronic jaundice from gall-stones.

With regard to 5. Enlargement of the spleen is rare with carcinoma, but common with gall-stone jaundice. In some cases it may be connected with a diffuse hepatitis which complicates the cholelithiasis, but this is by no means always the case. The splenic enlargement is not usually very great, the spleen being merely palpable below the costal border.

With regard to 6. In uncomplicated jaundice from gall-stones there is usually no ascites, unless there is general dropsy or peritonitis. I have seen it in two cases in which thrombosis of the portal vein was present in addition to a gall-stone in the common duct. With new growths in the biliary passages and with carcinoma of the pancreas ascites is not uncommon, and also when there is a diffuse hepatitis as a complication.

With regard to 7. The fever of cholelithiasis has been fully dealt with in other portions of this work. When chronic jaundice is present, the existence of fever, and especially the occurrence of rigors, is greatly in favour of the diagnosis of gall-stones, which in such cases may, of course, be complicated with suppuration in the biliary passages or in the liver. Nevertheless in cases of new growth in the liver, even when gall-stones and jaundice are absent, fever and typical rigors may be present. Hampeln and Anker have called attention to this point, and I can contribute the following example :—

CASE XII.—Frau M—— to the end of her 40th year had always enjoyed good health, but for some months past had suffered from an intractable intermittent fever. A severe rigor occurred every afternoon at about 4 o'clock, followed by a hot stage and sweating. During the attack the temperature frequently rose to 40° (104° F.) or higher. Lately there has been great anorexia and loss of power. Examination revealed conspicuous enlargement of the liver, in which, however, no nodules were felt. The gastric contents were of normal character; no fermentation; hydrochloric acid present. The left kidney is movable, and lies below the left costal border, being considerably pressed downwards towards the true pelvis. It can easily be displaced, is easily felt by bimanual palpation, feels hard and irregular, and is but little sensitive to pressure.

To the patient the rigors were intolerable, and she longed to be relieved from them at any cost. The removal of the kidney was suggested and accepted. As there was an idea of new growth in the liver the removal

was effected by anterior laparotomy (by Dr. Stetter, of Königsberg). Nothing abnormal was seen in the liver, and therefore nothing stood in the way of the extirpation of the kidney. This organ proved to be occupied for the most part by a whitish mass almost as large as an apple, which was shown by microscopic examination to be a sarcoma. No metastases were noticed. The patient made an excellent recovery. The rigors ceased, and the patient recovered.

Four weeks later, when the abdominal wound was already completely healed, the fever returned in the old way, with rigors each evening, followed by hot stage and sweating, and rise of temperature to 40° or 41° C (104° F.). The patient died from exhaustion. At the autopsy a large mass was found occupying a central position in the liver, exactly like the nodule in the extirpated kidney in character. There were metastases in numerous mediastinal and retroperitoneal lymphatic glands. Suppuration was nowhere found.

With regard to 8. This point has been already discussed on p. 107. Jaundice from new growths is sooner fatal, but even jaundice from gall-stones rarely lasts so long as a year.

3. *Infective Diseases of the Biliary Passages, and Hepatic Abscess, with Cholelithiasis.*

(*a*) *Cholangitis.*—I have already referred on several occasions to the ease with which infection of the bile takes place in cholelithiasis. The results of such infection are manifested in two very conspicuous affections of the bile passages, viz., cholecystitis and hepatic abscess. Both affections are brought about through cholangitis, and, in this role of intermediary, cholangitis is of the greatest importance, whereas in itself it is less often of much significance.

The *bacterium coli commune* appears to be the agent of primary infection in calculous cholangitis, and in cases of recent cholangitis, which are investigated by recent bacteriological methods, this bacillus is almost always found. It causes (conf. Experiments on Dogs, p. 48) exudative inflammation of the biliary passages and hepatitis, but does not necessarily produce suppuration. In dogs there is a complete absence of any admixture of pus with the bile, even although such bacillary cholangitis may prove fatal by general infection of the organism. Even in the cases of purely bacillary cholecystitis which I have observed and which are fully related in the next section, the fluid contained in the gall bladder was only slightly purulent. When there is actual suppuration in the biliary passages or in the

liver with cholelithiasis, staphylococci or streptococci have often been found in addition to Escherich's bacillus, as by Netter and Martha, Brieger, Rovighi and Leyden. Even in some instances of this kind Escherich's bacillus has alone been found (Netter and Martha, Gilbert and Girode, Bouchard, E. Levy).

As has been mentioned, infective cholangitis, as a rule, only attains to importance through its sequelæ, viz., cholecystitis or hepatic abscess, but there are cases in which uncomplicated cholangitis leads to general infection, and so proves fatal. Netter and Martha have brought together one case of their own and four under other observers, in which as a result of biliary obstruction, usually due to gall-stones, but in one instance associated with carcinoma of the biliary passages, acute endocarditis with a fatal termination was developed.

In the case personally observed by Netter and Martha there was purulent cholangitis in a few small intrahepatic ducts, and in the pus from the bile ducts and in the vegetations upon the cardiac valve-curtains the same bacillus, probably that of Escherich, was present. Abscess formation around the bile ducts in the liver, although not completely wanting, was in this case insignificant. In a case more recently reported by Rothmund from Eichorst's Clinic (Case X.), not only abscess formation in the liver, but also suppuration in the bile ducts appears to have been wanting. Here also death resulted from acute bacterial endocarditis (*endocarditis ulcerosa*).

On the other hand, purulent cholangitis is by no means rare in connection with cholelithiasis, and, especially when calculi are contained in the hepatic ducts, the passages in which they are present often contain pure pus, or purulent material mixed with bile or with precipitates of bilirubin-calcium. Again, when large gall-stones are impacted in the large bile ducts, pure pus, or pus mixed with the débris of concretions, is very commonly present in the spaces between the calculi, or between the calculi and the duct walls. Occasionally the entire system of bile ducts, from a calculus which occludes the common duct up to the ultimate radicles of the hepatic duct within the liver, are found filled with pus. Kussmaul describes such a case.

After cholelithiasis of many years' duration, and 3 weeks of fever with jaundice and rigors, the patient succumbed to

marasmus. At the autopsy the hepatic duct was found blocked by a concretion. Its branches and the intrahepatic ducts were dilated throughout. They formed a system of mutually communicating sinuous cavities varying from the size of a millet-seed to that of a cherry-stone. Within the liver, near its hilus, these cavities were so abundant that the liver "resembled a bath-sponge with larger and smaller perforations." These cavities were filled with bile-stained pus, and their walls consisted of a distinct membrane with a ragged surface; the liver tissue was dry and jaundiced.

When not entirely latent, cholangitis runs the course of a septic infection, behaving just like hepatic abscess, as Kussmaul himself says in speaking of his case. The only remaining symptoms dependent upon cholangitis are tender enlargement of the liver and, in some cases, jaundice.

(b) *Infective cholecystitis and empyema of the gall bladder (hydrops cystidis felleæ).*—Infective disease of the gall bladder frequently leads to empyema thereof. This occurs if the cystic duct is occluded, and the secretions of the mucous membrane, finding no channel of escape, collect in the gall bladder and cause its dilatation. At first the contents of the gall bladder consist of a mixture of the morbid mucous secretions with the bile which it originally contained. The constituents of this latter are somewhat rapidly absorbed, *i.e.*, in a few weeks at the longest, and the gall bladder then comes to contain a more or less purulent, seropurulent fluid. The quantity of pus corpuscles therein is usually small at first, and often remains so, even when the empyema has existed for a long time. In other cases true pus is met with sooner or later.

The bladder wall itself often participates in the disease, being the seat of inflammatory swelling, of œdema, or even of phlegmonous infiltration. In empyema the gall bladder may undergo a very remarkable degree of dilatation. There are undoubted cases in which the gall bladder contains a litre of pus, and it often contains as much as half a litre, and under these circumstances the dilated bladder fills the right half of the abdomen, more or less down to the concavity of the ileum.

The immediate cause of such exudative cholecystitis, viz., empyema of the gall bladder, is to be looked for, as already mentioned, in the infection of the bile, for the occurrence of which

cholelithiasis is as a rule responsible. Cases of empyema in the production of which cholelithiasis has no share are of rare occurrence. Courvoisier found this cause absent in only fourteen out of fifty-five cases of empyema. In most instances there is obstruction of the cystic duct or of the neck of the bladder, and less frequently of the common duct, by a calculus ; or at any rate calculi are present in the bladder itself.

Dropsy of the gall bladder results from occlusion of the cystic duct or neck of the bladder (almost always from impaction of calculi) when there is no infection of the bile, or after the infection has been removed. Here we have to do with the accumulation in the gall bladder of completely non-purulent fluid, rich in mucin.

In two such cases, in which I made a bacteriological investigation, the fluid was sterile. As an interesting constituent it contains cholesterin, always in small amounts, which frequently separates out in the form of glistening crystals. The change which the mucous membrane of the gall bladder usually undergoes in dropsy is also interesting, the epithelium losing its cylindrical character. In several cases I have found in its place an epithelial layer consisting of much larger cubical cells. Pitres and others have previously made the same observation. The dilatation of the gall bladder in dropsy may be very great, even exceeding the size of a child's head.

Cholecystitis is quite an ordinary occurrence in cholelithiasis. Indeed the enlargement of the gall bladder in regular gall-stone colic, when it reaches a high degree, is very often due, not to a mere distension of the gall bladder due to biliary obstruction, but to an infective exudative cholecystitis. The following five cases illustrate this :—

CASE XIII.—Female, aged 50. History : Apart from the diseases of childhood the patient had had no important illness, and in particular had never suffered from jaundice or colic. She had passed through nine parturitions, which all ran a favourable course. The catamenia last appeared in February of the current year. On Friday, October 31st, she was seized during the evening with very severe pains in the right hypochondrium, which lasted through the night, but disappeared next morning, and she then felt quite well again, and continued so until yesterday, when she was again attacked with cramplike pains more severe than the previous ones.

Present condition : The patient, who is of medium height, and fairly

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well nourished, lies rather sunk down in the bed. Expression anxious. The skin of the face is slightly flushed, and neither it nor the sclerotics are jaundiced. Temperature 38·2° (100·8° F.); pulse 94, irregular, of high tension. Artery rather hard, somewhat tortuous. The patient complains of very severe pain in the right hypochondrium. On examination there is felt, about a hand's breadth below the costal border, a smooth and rounded tumour about as large as a fist, which is very tender on palpation, and accompanies the liver in its respiratory movements. Above it is continuous with the liver, which is not particularly hard, and is likewise tender. The lower border of the liver could not be clearly made out, owing to the great tenderness on palpation. The hepatic dulness commences at the sixth rib, and in the nipple line reaches to more than a hand's breadth below the costal border. The spleen is not palpable, and its dulness is not increased. Thoracic organs normal; urine clear, free from bile pigment and albumen.

November 4th: During the night the patient was almost free from pain, and slept for several hours after 0·01 gramme (circ. gr. $\frac{1}{6}$) morphia. This morning the pains were again more severe; the tense tumour is to be felt as yesterday. At 11 a.m. an exploratory puncture was made, which yielded a clear fluid, obviously coloured with bile and rich in albumen, which showed under the microscope few formed elements, but was rich in small diplococci (on inoculating on gelatine a clear culture of Escherich's bacillus was obtained). After the puncture the pain attained to very great severity; the patient appeared somewhat collapsed; the pulse was 102; tension less than formerly; 0·02 gramme (circ. gr. $\frac{1}{3}$) of morphia was given. The pain abated in about 2 hours and the patient slept. In the evening the pain was less; the tumour was unchanged, being as tense as before the puncture. About 300 cc. (10$\frac{1}{2}$ ozs.) of urine were passed; sp. gr. 1025; no albumen. Medicine ordered: inf. rad. rhei 5·0 in 180 cc. (31$\frac{1}{2}$ in 6$\frac{1}{2}$ ozs.) of water; poultices.

November 5th: The pains are less to-day; tumour unaltered; pulse rather quieter, 90 per minute, still with frequent intermissions. At mid-day a free evacuation after an enema. Medicine, 3 grammes (circ. gr. 46) of sodium salicylate. Skin and sclerotics not jaundiced; urine free from bile. Evening temperature 39·2° (102·6° F.). At 9 p.m. a rigor lasting about half an hour.

November 6th: Patient slept well last night; is to-day free from fever and pain. Pulse less tense, 80 per minute, not intermittent; urine more abundant, 800—1022 cc. (31$\frac{1}{2}$—39 ozs.), without albumen, no Gmelin's reaction, no indican, no jaundice.

November 7th: Temperature last evening 38·6° (101·5° F.). Had a good night; slept better than before. Patient feels very well to-day; the tumour can be palpated without pain. The pulse feels almost normal. Evening temperature 38·2° (100·8° F.). The pulse remains more regular and quieter this evening, although more rapid than in the morning (94 per minute).

November 8th: The subjective well-being continues; no further attacks of pain. A formed motion of good colour has been passed.

Abundant diuresis; no albumen or bile-pigment reaction in urine. No trace of cutaneous jaundice.

November 9th: Temperature no longer raised, even in the evening. The tumour appears to shrink, or at least is less tense. No stone was found in yesterday's motion.

November 11th: Improvement continues. Patient looks better. The tumour is obviously diminishing, its lower edge being almost at the level of the umbilicus. A moderately soft extension from the liver, of about the breadth of a hand, extends from the costal border as far as the tumour, which is no longer clearly marked off from the lobe of the liver. Neither at the outer or median side can the lower border of the liver be marked out above this apparently isolated lobe.

November 12th: Slept well. Motion formed and of good colour; urine abundant.

November 15th: Patient feels quite well; has no more pain; in the normal motions, passed about twice a day, no stones were present. Temperature and pulse remain normal. The position of the tumour as on November 12th. (Enema; no stone in motion.)

November 18th: Patient continues free from pain; the tumour has further decreased, and its lower border is palpable a finger's breadth above the navel as a moderately hard resistance, disappearing towards either side, and not to be marked off from the liver, which extends for about a hand's breadth beyond the costal border. No tenderness on palpation.

November 20th: Patient was quite well yesterday, and also slept well on the previous night. This morning the tumour appeared somewhat larger, but is not painful. About noon very severe colicky pains came on, which quickly reduced the patient to a condition of great exhaustion. The pulse was again very irritable, intermitting every third, and often every second, beat. The gall-bladder tumour rapidly increased to the size which it had on the day of the first attack. In the evening, at about 6 o'clock, the tumour again extended a hand's breadth below the navel, lay against the abdominal wall, was very tense, and extremely tender on palpation. Poultices and injections of morphia (two of 0·01 gramme) reduced the pain, but the patient remained much exhausted and upset, and passed a sleepless night.

November 21st: Slight improvement. No colic pains, but great tenderness on palpation of the tumour, which retains its size. General weakness. Pulse very unsteady, not accelerated (about 86), frequent intermissions; urine scanty (about 400 cc. (14 ozs.)), clear, pale yellow, gives no bile-pigment reaction, and contains no albumen. In the afternoon a formed motion passed, brown in colour, containing no calculus.

November 22nd: Last evening patient took 3 grammes (circ. gr. 46) of sodium salicylate. She had a good night, and to-day the tumour is rather smaller, reaching only a little way below the navel, and is less painful. General condition still conspicuously low and depressed. Pulse as irregular as yesterday; no jaundice.

November 23rd: Gradual improvement of the general condition.

Patient is picking up. Pulse still conspicuously intermittent, after four rapid beats there follow two slower ones, with twice the interval between them (due to the intermission of a beat). Towards evening, soon after 6 o'clock, the irregularity of the pulse increased, and the patient felt very ill. The weakness, which resembled collapse, became almost alarming. The pulse was slowed, 60—70 per minute, and very intermittent. Respiration about 26 per minute, deep and laboured. The patient sits up in great anxiety, on account of the tightness at the chest, but soon falls back exhausted from sheer weakness. No hepatic pains, and no tenderness on palpation. Four injections of caffein given, 0·2 gramme (circ. gr. 3) every half-hour. Towards night the pulse improved somewhat, the breathing was quieter, but the patient did not sleep, but remained all night in a half-awake exhausted condition, and was restless and anxious.

November 24th: The heart's action is to-day much quieter than last evening; the pulse less intermittent, about 80 per minute. The tumour, situated at the level of the umbilicus, is less tense and not tender. There is no jaundice. Urine scanty, free from bile pigment and albumen. In the afternoon a small formed stool was passed, containing no calculus.

November 25th: After a good night's rest, and feeling decidedly better this morning, the patient, who dreaded an operation that was suggested, was removed from the institution by her friends. Since the 4th of November there had been no febrile disturbance.

CASE XIV.—A woman, aged 49 years.

December 7th, 1891 : History—The family history showed nothing remarkable. About 8 years previously she had suffered from peritonitis, but had otherwise been quite healthy. In the night of the 3rd and 4th of December, *i.e.,* 3 days previously, she was suddenly seized with acute pains in the epigastrium, which radiated to the back, shoulders, and legs. She was compelled to vomit, and the vomited matter was fluid, and black and green in colour. Then the pains became more severe, and have maintained their intensity to the present time. The pains were most intense in the right hypogastric region. The patient seems to have had fever, but no rigor. She has always been constipated, and has had no motion since the 3rd instant. The patient had borne seven children normally, the last 7 years ago. Four children are alive and healthy.

December 8th: Present condition—A medium-sized, well-built woman, but ill nourished. Complexion pale; expression suffering. No fever, no œdema, no jaundice. Pulse 76, small; moderate tension. Thoracic organs normal. Abdomen much distended ; the right side does not move at all with respiration, the left only slightly. The right side appears somewhat more tense than the left. The entire abdomen, and especially the whole of the right side, is painful and tender on pressure. A resistance is felt, which cannot be accurately defined on account of the great tenderness, but which is most marked in the hypogastrium, and

does not extend across the middle line. Over this there is a modified tympanitic note; anorexia; urine contains no albumen or bile pigment, but much indican; bowels not open.

December 8th : The patient is taking 0·06 gramme (circ. gr. i.) of extract of opium daily. This morning she vomited, bringing up liquid with green coloured lumps. The abdominal pain is somewhat less. The urine contains much indican. *Per vaginam* a tumour is felt high up in the vaginal fornix, which can be only incompletely palpated.

December 9th : The pains are somewhat less, otherwise no change.

December 10th : Patient was suddenly unable to pass her water to-day, and catheterisation was necessary. Urine contains no albumen; pains only slight, but still present. The tumour in the ileo-cæcal region can be clearly felt to-day. It is moderately firm, the size of a man's fist, and yields no fluctuation. The urine contains much indican.

December 11th : As the patient is almost free from pain the tumour can be clearly defined to-day. It is about the size of a fist, and somewhat rounded below. Above and to the outer side it extends beneath the costal arch; its lower limit lies a hand's breadth above the pubes, and on its inner side it extends to the middle line. On light percussion impaired resonance, but on stronger percussion the note over the tumour is of a modified tympanitic character. The tumour does not move with respiration. It is firm, elastic, and yields in one spot ill-defined fluctuation. Firmer pressure upon it causes pain. This morning the bowels were open spontaneously. The motion was of a good, firm consistence, and contained bile pigment. She was no worse after it. The tumour feels still more defined than yesterday, and is not clearly limited on its outer border. Below it has a globular fundus a hand's breadth above the symphysis. No movement with respiration. No jaundice. An exploratory puncture yielded a syringeful of clear, pale, brownish-yellow, thin liquid; which contained mucin and a considerable amount of albumen; gave the reaction of bile pigment, and had no fæcal odour. From this fluid *bacterium coli commune* grew in pure cultures in considerable quantity (showing the characteristic growth on potatoes, and causing acute fibro-purulent peritonitis in rabbits). In the afternoon the catheter was required, as the patient could not pass her water. Urine quite clear. The tumour was painful on hard palpation. No vomiting.

December 15th : The pains have completely disappeared. General condition excellent. The tumour is quite clearly palpable, has the form of the gall bladder, is firm and elastic, and now yields distinct fluctuation. To-day it moves distinctly with respiration.

December 20th : Although otherwise comfortable, the patient has, during the last few days, complained several times of painful defæcation. The abdomen is flat, and the tumour has decreased in size from day to day, and there has been no attack of pain. There is still no distinct limit of the tumour in the region of the gall bladder. The abdominal muscles, especially the rectus, are still more contracted upon the right side than on the left, and consequently there is more resistance on the

right side than on the left. No distinct dulness on hard percussion, and only on light percussion with the handle of the plessor is slight impairment made out in the region of the gall bladder. There has never been any jaundice, or bile pigment in the urine; the motions have always contained bile pigment. The lower border of the liver is palpable. On percussion the liver extends beyond the costal arch to about the breadth of the plessimeter, outside the nipple line.

December 21*st:* The patient passed a fairly copious motion last evening, for the first time, after an enema, and this contained bile pigment. No gall-stones were found. During her stay in hospital there was never any fever. On account of the distinct peritonitic symptoms, the case at first simulated circumscribed peritonitis (perityphlitis). The rapid recession of all the symptoms, and the results of the exploratory puncture, left no doubt, however, that the case was not one of peritonitis from perforation, but of undoubted calculous cholecystitis with peritoneal irritation.

CASE XV.—A washerwoman, aged 48.

November 21*st,* 1890 : History: The patient comes of a healthy family, and is said to have had no previous illness. About fourteen days ago she was suddenly seized with acute pain in the right leg, especially in the calf, so that she dragged the leg. In the night, between last Sunday and Monday, the patient woke, and felt an acute pain, first in the chest and then in the right side, which has not yet left her. At the same time the pain in the leg disappeared. Patient is fairly strong. There is slight jaundice of the skin and sclerotics. Nothing remarkable in the lungs or heart. Abdomen slightly swollen, and evenly distended. Liver-dulness commences at the fourth inter-costal space, and its lower border is two fingers' breadth below the costal arch. At this level there lies, between the nipple and anterior axillary lines, a fairly hard, but somewhat elastic, tumour, of the size of a goose's egg, rounded, symmetrical, and easily defined by palpation, except at the upper part, which sinks with inspiration and rises, and cannot be retained in its lowest position during expiration. The tumour is moderately firm and somewhat tender. Spleen not markedly, but probably somewhat, enlarged. In the remaining organs there is nothing abnormal ; no febrile disturbance.

December 7*th:* The stomach was distended with CO_2. The tumour was greatly displaced towards the right and upwards.

December 8*th:* An exploratory puncture yielded a faintly tinted, highly fibrinous fluid containing a few leucocytes, and no peculiar formed elements. From this *bacterium coli commune* was obtained in pure cultures.

December 16*th:* The tumour of the gall bladder has been no longer clearly palpable or defined for several days, although there is still pain in its region. Patient's appetite is good, and her condition excellent in other respects. Bowels open regularly. No calculi found.

December 20*th:* The tumour has not again become distinct, and since

the patient suffers practically from no discomfort, beyond a slight feeling of discomfort, like pressure, in the hepatic region, the operation originally proposed was abandoned.

December 26th: The patient was discharged with no discomfort, in excellent general health. The tumour has not again become evident. No gall-stones were found.

CASE XVI.—Cook, aged 31 years.

History.—Of the parents of the patient : the father died of inflammation of the lungs; the mother is living and in good health. The patient had measles and scarlet fever in childhood, but has otherwise always been healthy. Her present trouble began a fortnight ago with tearing pain in the hepatic region, accompanied by severe vomiting and occasional rigors. The pain often concentrated itself upon a single point, as if boring through the abdominal wall.

December 8th: Present condition.—Slight jaundice of the conjunctivæ, a considerable prominence in the right hypochondrium, and on palpation a soft, painful tumour, which cannot be distinctly defined.

The tumour appears to become firmer under the palpating finger, and afterwards the contraction passes off. The tumour, which has a median diameter of about 15 centimeters, lies to the outer side of the right nipple line. In the upwards direction it extends to the border of the liver, and the liver itself is also tender. The spleen is clearly palpable; the splenic dulness begins at the seventh rib in the central clavicular line, and can be traced forwards over the costal border. Thoracic organs normal. No distinct bile-pigment reaction in the urine; no albumen. Morphia and poultices were ordered.

December 10th: Exploratory puncture. A fairly clear fibrinous fluid was removed, rich in albumen and containing some mucus. At 1 o'clock a severe rigor with pain in the region of the tumour.

December 15th: The tumour has decreased in size from day to day, and to-day can hardly be clearly felt. A slight prominence is still noticeable in the region of the gall bladder.

December 17th: The tumour is again clearly defined to-day, and has the same limits as before. In the afternoon an attack of severe pain. Fæces examined for gall-stones; none found.

December 19th: The tumour is again hardly felt. The patient was transferred to a surgical ward; but in the course of a week the swelling completely disappeared, there was no discomfort, and therefore the operation was abandoned. There was only slight fever in the early days in this case.

CASE XVII.—A woman, aged 33.

History.—The patient's mother died of cancer in the stomach at 47, and her father of consumption at the same age. The patient was always healthy as a child, and menstruated at the age of 15. The periods were always slight, and during the first years recurred every fortnight. She married at 24. Between her 19th and 25th years the patient frequently suffered from rheumatism.

The patient had borne five children, the last on November 26th, 1889. Of the children two have died (of convulsions and diphtheria). The last child is healthy, and she has suckled it up to the present time.

The present illness commenced on Sunday, October 19th, 1890.

After feeling quite well all day she was attacked in the evening with severe abdominal pains and vomiting. Since then she has almost immediately vomited all food that she has taken. The bowels were opened naturally on Sunday evening, and on Monday morning after an enema. Up to then the motions were natural, but early this morning diarrhœa set in. There had never been any jaundice.

Present conditions.—Patient is strongly built, of pale appearance. No jaundice of skin or sclerotics. The visible mucous membranes are pale. Tongue covered with a white fur. No enlarged glands in neck. Pulse 108, regular, of moderate tension. Abdomen slightly tumid; numerous scars of pregnancy. Epigastrium retracted. To the right of the navel slight tumidity. Palpation reveals, on the right side, between the sternal and nipple lines a deep-seated tumour, of elongated oval shape, of the size of a fist, with its long axis parallel to the middle line. The tumour feels somewhat uneven, and moves up and down with respiration. It can also be easily shifted by palpation. In the dorsal position its lower limit reaches to a line connecting the anterior superior spines of the ilia. When the recti are relaxed the median border of the tumour also is clearly felt. The upper border towards the liver cannot be made out. The lower border of the liver does not distinctly come below the costal border. Between the sternal and nipple lines there is a direct transition from the liver dulness to the slightly dull tympanitic note over the tumour. The tumour is somewhat tender on pressure on the median side. It falls towards the left when the patient lies on that side, and at the same time the note becomes more resonant towards the right. No enlargement of the spleen can be made out by percussion, nor is that organ felt. The contents of the stomach are coloured with bile, are fluid, and strongly acid, but give no distinct hydrochloric acid reaction. The bowels are only open after enemata, and the motions are loose and blood-stained. Urine is concentrated, sp. gr. 1033. The amount reaches 800 cc. (26 oz.), it contains much albumen and indican, together with pale hyaline and a few granular casts. The patient complains of spontaneous pains in the abdomen and vomits after all food.

October 25th: An exploratory puncture was made to-day. A syringeful of slightly fluorescent fluid was removed, which on microscopic examination was found to contain numerous leucocytes and red blood corpuscles.

On the addition of acetic acid a turbidity resulted (mucin).

After the puncture the patient had acute pain, and became slightly collapsed; the pulse was rapid and small, and the face, skin, and mucous membranes became pallid. Cold sweating also occurred. After a few hours the patient revived, but still complained of acute pains.

October 27*th* : The patient has no pain when at rest, but on movement some pain is still felt at the seat of puncture. The tumour is unaltered.

October 28*th* : The urine is free from albumen to-day. Sp. gr. 1026; its tint is pale yellow.

November 4*th* : The urine is still free from albumen. A few hyaline casts are present. No more attacks of pain. No vomiting.

The patient left the hospital at her own wish, since she could not make up her mind to submit to an operation.

In all five cases one had to do with first attacks of gall-stone colic, and quite recent enlargement of the gall bladder. The puncture of the gall bladder was performed within a few days, and in the longest instance three weeks, after the commencement of the illness, and in no instance was actual bile obtained. In one case only was the fluid obtained still obviously bile-stained, and even in that instance the inflammatory nature of the exudation was made evident by the presence of much albumen. In the four remaining cases the fluid removed showed hardly any distinct biliary colouration, but in one case it gave the bile-pigment reaction, and in two the microscope showed scanty precipitates of bile pigment. In all cases the fluid was only slightly turbid, contained little mucus, but obviously contained albumen, and a considerable number of white, together with a few red, blood corpuscles.

In three out of the five cases the fluid removed contained the *bacterium coli commune* (Escherich's bacillus) in abundance, and one saw the short rods and double rods even in stained or unstained preparations made direct from the fluid itself. In plates moistened with the fluid, ten times diluted, there grew innumerable and closely packed colonies. In one case the fluid, though similar in other respects, was sterile. In the last case (No. 17) no cultures were made.

In all these five cases cholecystitis commenced with an attack of gall-stone colic. In four jaundice was completely absent, but in one slight yellowness of the sclerotics was noted. In all these cases then the stone probably lay in the cystic duct.

In several cases the character of the illness was, except for the presence of gall-bladder tumour, determined by the biliary colics. These ran a typical course, and when they ceased all was at an end, save for the swelling in the right hypochondrium, which persisted for a time. The enlargement of the liver was no

greater than that usually associated with gall-stone colic.
There was never more than a slight enlargement of the spleen,
which was recognisable by palpation in only one instance.
Febrile disturbance was trifling, or altogether wanting. Rigors
occasionally occurred, but were not of exceptional severity. The
enlargement of the gall bladder was in each case very consider-
able, the bladder reaching down to, or even below, the navel
during the height of the attack. Under these circumstances it
was always very tender, and often spontaneously painful when
the patient was at rest. In one instance (Case XIV.) the pain
felt during rest radiated over the whole of the right hypogastric
region ; and in this region the abdomen was so sensitive to
pressure, the muscles were so rigid, the respiratory movements
of the right half of the abdomen were so restrained, and the
collapse was so pronounced, that on the first day the diagnosis
of perityphlitis was arrived at after a careful examination.

As a rule the pain in the swollen gall bladder disappeared
completely in the course of a few days, and then the swelling
always diminished, and at first somewhat rapidly. In one
instance, after an interval of three days, a fresh colic attack
was followed by renewed swelling and tenderness of the gall
bladder.

The course of the disease was not unfavourable in any of
these cases, but it is probable that in all of them the calculus
remained permanently incarcerated in the cystic duct. In favour
of this view is the fact that in the majority of the cases the gall-
bladder tumour was still present when the patient, rejecting
the advice offered, left the hospital without being operated
upon. Even in the cases in which the tumour ultimately
disappeared entirely, the reduction of size was so gradual that
this event was to be ascribed to reabsorption of the contents of
the gall bladder, rather than to freeing of the cystic duct.

It would appear that such cases of acute cholecystitis
associated with gall-stone colic, which are certainly very
common, have been usually looked upon hitherto as examples
of simple distension of the gall bladder due to accumulation
of bile. Courvoisier states, indeed, that when swelling of the
gall bladder occurs in attacks of colic, exudation occasionally
has a share in its causation. He also mentions empyema of
the gall bladder "running an acute and even a hyperacute

course." The very few cases of this kind available have, according to this author, all run a fatal course within a few days. My cases by no means justify so evil a prognosis, yet I am convinced that cholecystitis is a very serious complication of gall-stone colic. Death may follow as the result of peritonitis. Potain had a case of this kind under his observation, in which cholecystitis was fatal in two days by peritonitis. There was no perforation of the wall of the gall bladder, but the inflammation, having its origin in the gall bladder, had extended from the mucous to the serous membrane through the intact wall. In one of my cases (No. XIV.) threatenings of peritonitis were present. In other instances death has quickly resulted, with the symptoms of general infection.

CASE XVIII.—A married woman, aged 69 years.

October 7th, 1891: She does not know the diseases from which her parents died. One brother is alive and is healthy. The patient says that she has had no previous illness. At the age of forty she passed through an attack of " child-bed fever "; she has borne six children, of which one only is alive; she has worked in a tobacco factory, where she has always sat at her work. For some time she had occasionally suffered from abdominal pains, which disappeared after taking " China wine "; she vomited frequently and lost her appetite completely; frequent constipations.

Present conditions.—Tall, strongly-built woman, with stout bones and well-developed *panniculus adiposus*. The skin has a lemon-yellow tint, and the sclerotics are also yellow. Pulse small, irregular, and frequently intermittent. Heart shows nothing abnormal; lungs normal. The abdomen moderately distended, with dulness in the dependent parts. On the right side the liver dulness reaches to the lower border of the ribs. The edge of the liver is difficult of palpation owing to the excess of subcutaneous fat, but nevertheless it seems to be somewhat distinctly enlarged on palpation. Beneath the right costal arch, to the outer side of the parastenal line, a hard round tumour is felt, freely movable, and moderately tender when touched, which moves downwards with inspiration. The limits of the splenic dulness cannot be made out. The urine is very scanty, turbid, and of a greenish colour; it contains much albumen, granular casts, and casts with cells attached. Its reaction is strongly acid, and it yields the bile-pigment reaction. Sensorium much disturbed, consciousness impaired.

October 8th : An exploratory puncture of the tumour in the region of the gall bladder yielded a syringeful of turbid fluid, thin and not coloured by bile. Microscopically it contained, in addition to detritus granules, pus cells, groups of fat granules, a few epithelioid polygonal cells, with large round nuclei, arranged in groups (liver cells?), and

bacterium coli commune in pure culture. Yesterday afternoon the patient became greatly collapsed, and was consequently given four doses of 0·1 grm. (circ. 1½ gr.) of musk. The pulse was extraordinarily feeble and irregular.

This morning the extremities were cold, the pulse intermittent and extremely feeble, and the expiration irregular. Caffein-sodium salicylate three doses of 0·2 grm. (gr. 3) subcutem. A few cc. of greenish-black urine were drawn off with a catheter (rich in albumen and casts).

October 10th : Patient's condition has improved somewhat. Jaundice continues unaltered; pulse very irregular; heart sounds scarcely audible. She cries and calls much, and is not fully conscious. The anuria is almost complete; even with the catheter only a few cc. could be drawn off. Dulness in the dependent parts of the abdomen to-day, but the dulness does not distinctly shift. No diffuse tenderness; the region of the gall bladder is alone somewhat painful on pressure. The tumour there is still unaltered; elsewhere the abdomen is moderately distended and soft. A grey stool, free from bile, was passed.

October 11th : The patient has passed no urine during the last few days, and by means of the catheter only a few cc. of a thick, greenish-black urine could be obtained. The passing of the catheter appears to cause pain.

October 13th : The patient has passed copious bile-free motions under her, and this morning the bed was very wet also, so that an abundance of urine must have been passed, and this appears to have been less deeply bile-stained than previous specimens. The gall-bladder tumour, which to-day felt large, lightly distended, and hard, was punctured this morning with a very fine trochar and cannula after the abdominal wall had been disinfected. About 100 cc. (circ. 3½ oz.) of a clear, pale yellow, and somewhat viscid fluid escaped drop by drop. At times this was slightly blood-stained. That which came away at the end was more turbid, and contained many leucocytes, groups of fat granules, and diplo-bacteria. The addition of acetic acid produced a flocculent precipitate which was not soluble in excess. The patient is very apathetic, and has ceased to take nourishment.

October 14th : The patient is still very restless to-day; takes nothing at all. Passes urine and motions into the bed. At times, as on the previous days, there is singultus, but no other symptom of peritonitis. The gall bladder can be distinctly felt, but is less tense than yesterday.

October 15th : The patient died this morning at about 9 o'clock, after a very restless night. An extensive bedsore has developed over the sacrum during the last few days. The patient had no fever throughout her stay in the hospital.

Autopsy.—Embolism of the left *arteria profunda cerebri*, with softening of the left occipital lobe, and a patch of softening the size of a cherry in the third (?) left frontal convolution. An old cardiac aneurism, no recent endocarditis. Spleen not enlarged; contains a recent infarct. In the left lobe of the liver two fresh abscesses the size of walnuts. Gall

bladder large, adherent to the colon, showing incipient perforation. It contained several facetted calculi of the size of cherries, and some turbid green fluid. The hepatic and common ducts were patent. Mucous membrane yellow coloured. A carcinomatous stricture of the cystic duct at its junction with the common duct. All the bile ducts, even including those within the liver, dilated.

In the body of this elderly woman there were various lesions which were doubtless in part independent of each other, but there could be no question that there had been acute sepsis, having its origin in the acute bacillary cholecystitis.

Even when the course is a favourable one in the early stages, it is very probable that an infective affection of the gall bladder persists, which may again produce symptoms later. It may then take the form of a fresh acute cholecystitis, or the process may continue to pursue a chronic course.

It is, of course, by no means necessary that the development of calculous cholecystitis should go hand in hand with an attack of gall-stone colic. The cause of the cholecystitis is the infection of the bile in the bladder with *bacterium coli commune*, and it may develop whenever the bile becomes stagnant in the gall bladder. To produce this effect it is not necessary that calculi should be set in movement, but merely that the bile should be shut off. As a rule, indeed, calculi lying in the bladder are the cause of this, but cholecystitis is occasionally, though rarely, developed when no stones are present. Under certain conditions the diagnosis of acute cholecystitis from an attack of colic may be a matter of difficulty, as is evident from the Cases XIII.—XVII.

If the cholecystitis takes on a chronic course, the symptoms are very different. This condition may manifest itself as a definite inflammatory affection, or in the form of an indolent swelling of the gall bladder. Under such circumstances there may be febrile disturbances, usually of definitely intermittent type. The exacerbations of the fever may go hand in hand with painful enlargement of the organ, as in the cases described by Reipschläger and operated upon by Lücke (Kussmaul), often enough fever is entirely wanting.

Lastly, rupture, external or into the peritoneum, very frequently results, and the majority of biliary fistulæ have their origin in empyema of the gall bladder. The contents of the gall bladder in infective bacillus cholecystitis are, as is well

known, usually only slightly purulent at first. Nevertheless, true pus is ultimately found, as has been already mentioned when speaking of cholangitis.

The diagnosis of empyema of the gall bladder will usually be only possible when the distension of the gall bladder leads to the formation of a palpable tumour. Apart from this it is only quite exceptionally that favourable conditions lead to the diagnosis. For example, when a tumour of the gall bladder has been recognised at some previous time, one may conclude that empyema of the gall bladder is present when febrile disturbance and pains in the region of the gall bladder develop, even although the tumour has disappeared.

As a rule the diagnosis chiefly depends upon the formation of a correct estimate of the nature of the tumour in question, and consequently this appears to me to be the place in which to enter more fully into the diagnostic points of gall-bladder tumours.

(a) *The position of the tumour.*—Even when the tumour appertains to the gall bladder it may be deep situated in the abdominal cavity, and may be only very indistinctly palpable from the front. This is the case when, for example, the gall bladder has become adherent to the pylorus or duodenum, whether a fistulous opening has been formed or no. As a rule the gall bladder is quite to the front, just behind the anterior abdominal wall, and usually, but by no means always, it is easy to recognise that the tumour projects below the border of the liver, *i.e.*, the hepatic border can be traced from the right or left as far as the tumour, but can seldom be followed over the actual swelling. In any case the tumour cannot be distinctly defined at its upper border, whereas below it is hemispherical, ovoid, or sausage-shaped. Not unfrequently it is distinctly bent upon its long axis so as to resemble a cucumber in form. (This simile was first employed by Courvoisier.)

In such cases the fundus of the cucumber-shaped bladder, which is somewhat bent forward, may alone be felt as a tumour, situated superficially, and completely separated from the liver.

In this way the intestine may lie in front of the gall bladder, between its fundus and the hepatic border. (In a case operated upon by Lücke the transverse colon, and in a case under my own

observation, which came to an autopsy, a coil of small intestine was found in this situation. Lawson Tait has also seen a similar condition.)

As a rule superficial dulness (to light percussion), which passes into the liver dulness, is met with over the tumour. In exceptional cases of the kind just referred to, even this superficial dulness will be absent, or at any rate its connection with the liver dulness will not be evident.

When the tumour is connected with the gall bladder it usually lies in the parasternal line, i.e., by the outer border of the rectus abdomines, but conspicuous deviations from this position are met with. In cases confirmed by exploratory puncture, autopsy, or operation I have found the distended gall bladder situated to the outside as far as the nipple line, and in the other direction almost in the middle line. This latter deviation is in my experience rarer than the other.

I cannot, therefore, acknowledge the importance of Taylor's "diagnostic line." Taylor states that the enlarged gall bladder always lies in a line which, starting from the normal seat of the fundus of the gall bladder, i.e., from the anterior end of the cartilage of the tenth rib, runs downwards and to the left, so as to cross the middle line, slightly below the navel.

(b) *Mobility.*—As a rule the movements of the tumour with respiration are very evident in empyema and dropsy of the gall bladder. They may be temporarily in abeyance where the tenderness is very great, and in such cases there is not necessarily any adhesion between the gall bladder and the anterior abdominal wall. Lateral mobility is usually best marked in cases in which the tumour projects some distance below the border of the liver. In the anterior-posterior direction also it is freely movable, and where there is only slight swelling it often distinctly evades the palpating finger.

The tumour may also as a rule be readily pushed upwards, but does not remain displaced (as the kidney does), for I have always seen it immediately return after such displacement and resume almost exactly its original position. In various positions of the patient's body the tumour often shifts its position conspicuously and rapidly. In its behaviour during deep respiration a tumour of the gall bladder sometimes differs very markedly not only from a floating kidney, but also from

omental, intestinal, and even gastric tumours. The swollen gall
bladder sinks downwards on inspiration, and rises once more
on expiration, and these excursions cannot be arrested, even
when it is possible to take hold of the tumour. Tumours of
the kidney, stomach, omentum, or intestine are likewise often
depressed on inflation, but in many cases it is possible to
prevent the upward movement during expiration by grasping
the tumour, or by rapidly pressing the fingers against its
upper border, when its lower level is reached.

(c) *Behaviour of the tumour on bimanual palpation, and when
the stomach and intestines are distended with gas.*—On bimanual
palpation, one hand being applied behind, in the right renal
region, the other in front, over the tumour of which the nature
is in question, one can often make out renal tumours very
clearly, and they can be in this way held between the two
hands. This is not the case with tumours of the gall bladder.
Nevertheless, great care must be taken that the hand which is
behind be not applied too far out, *i.e.*, not to the outer side of
the outer border of the quadratus lumborum, for if this pre-
caution is neglected tumours of the liver and gall bladder can
be bimanually felt, and so an erroneous conclusion may be
arrived at.

Sometimes it is very clearly shown to what organ the tumour
belongs by distending the stomach with gas (by means of an
effervescing powder). If it be the gall bladder, the tumour is
distinctly shifted towards the right and also upwards. At the
same time, provided that the increased tension of the abdominal
wall does not interfere, it is sometimes pushed more against
the anterior abdominal wall, and so becomes more distinctly
palpable. A renal tumour, on the other hand, if it be not
of excessive size, rapidly ceases to be palpable under such
conditions, and this will more certainly be the case if the
intestines be filled with water or gas.

In cases in which the intestine intervenes between the fundus
of the gall bladder and the liver, this can sometimes be made
evident by the inflation of the bowel, as in Winkelmann's
(Lücke's) case, and in that which I observed.

(d) *The nature of the contents of the tumour* can be ascer-
tained by an exploratory puncture, and the information so
obtained is often of great value. Courvoisier's statement

is certainly correct that, in empyema and dropsy of the gall bladder, the contents are usually free from bile staining, and therefore their nature does not in itself afford proof that the tumour is one of the gall bladder. The significance of the result lies in other directions, since it determines whether we are dealing with empyema, dropsy, or simple dilatation of the gall bladder, and frequently whether a carcinoma or a deformity of the liver due to tight lacing is simulating a tumour of the gall bladder.

One should, however, be careful not to make the puncture with a short needle, and not to puncture too far above the lower margin of the tumour, for if this precaution be neglected, it may happen that the gall bladder is not reached through the liver which covers it. If after repeated punctures of the tumour to be diagnosed nothing but blood is obtained, simple empyema and dilatation of the gall bladder can be excluded.

On the other hand, such a negative result is very frequently obtained with carcinoma of the liver and gall bladder. Pure bile does not point to cholelithiasis, but is more frequently obtained when obstructive jaundice from other causes is present. The diagnosis between empyema and dropsy is only safely made by an exploratory puncture. In dropsy the fluid is clear, and even on microscopical examination no pus corpuscles are found in it, but the characteristic pavement epithelium is sometimes present. In empyema pus corpuscles are never absent, and true pus, which may or may not be coloured by bile, is often obtained. Moreover, the fluid of empyema is always albuminous, whereas the fluid of dropsy usually contains no albumen, but abundant mucin. Mucin is usually present in empyema also. However, exploratory puncture is not entirely free from risk. The wall of the gall bladder is often very thin and tightly stretched, and its contents are often highly infective.

I have almost always thought that I have detected signs of slight peritonitic irritation after exploratory puncture in cases of acute cholecystitis, but with rest, morphia, rather tight bandages, and the ice bag these have always rapidly passed away without further ill effects. One should always proceed with great caution, the puncture being made with a needle of the smallest size, and only after one has convinced oneself

that no intestine lies between the tumour and the anterior
abdominal wall.

After what has been said I need not insist on the point, that
I regard the search for calculi by means of the exploring needle,
as it has been carried out by Harley and others, as a dangerous
proceeding, and one not to be recommended.

C. *Infective Hepatitis* (*Abscess of the Liver*).

In the livers of patients who have died of cholelithiasis,
suppurative processes are not very unfrequently met with.
Schröder found amongst the cases which he collected purulent
hepatitis in nine out of 144 autopsies. As a rule, there is merely
an insignificant purulent infiltration in the immediate neigh-
bourhood of one or other of the bile ducts ; but sometimes
there is very conspicuous suppurative hepatitis in association
with cholelithiasis, but even in such cases it does not often
determine the course of the disease. As a matter of fact,
a calculous abscess which is available for purposes of diag-
nosis or treatment is rare. Even in our climate (leaving
tropical abscess entirely out of consideration) the majority of
hepatic abscesses are metastatic. The most frequent cause is
perityphlitis, and, after this, other suppurative or ulcerative
processes in the region of the radicles of the portal vein.
Suppurating hydatid cysts too more frequently come to opera-
tion among us than do hepatic abscesses due to calculi, as is
clearly shown, for example, by the tables of Lawson Tait's
operations.—(*Edinburgh Medical Journal*, Vol. XXXV., 1889.)

Calculous abscesses coming to operation are indeed rarer than
the literature would seem to show, seeing that in many cases
which are operated upon as examples of hepatic abscess the
actual lesion is an empyema of the gall bladder, as, for example,
Rajgrodzki's case. This being so, many of the cases in which
gall-stones were evacuated from an "hepatic abscess" must be
regarded as open to question.

Occasionally there have been found in the liver, in connec-
tion with cholelithiasis, minute (miliary) abscesses, which are
usually multiple and of very varying sizes. The individual
abscess cavities may communicate with each other, either
directly or by dilated bile ducts, and in this way cavities may

be produced penetrating through the greater part of the liver. Thus in a case in my clinic the existence of a calculous abscess in the right lobe of the liver was demonstrated by an exploratory puncture in the eighth intercostal space in the anterior axillary line. No further operation could be performed because the patient sank too rapidly.

At the autopsy an abscess as large as an apple was found in the right lobe, which was in connection, by means of dilatation of the large bile ducts, with other abscesses, larger than apples, in the neighbourhood of the portal vein and in the left lobe. The entire many-branched cavity was filled with bile-stained pus, in which lay a few concretions. The contents of the abscess are sometimes pure pus, sometimes of an almost pure biliary green or brown-red colour, or show an intermediate tint. In many cases concretions are found in the abscesses.

In the cases in which there is incipient purulent infiltration in the neighbourhood of individual ducts, the ducts are not unfrequently found to be filled with brittle or soft masses of a dark greenish brown or reddish brown colour. In other instances the abscess cavity contains concretions of various sizes up to that of a nut. These are often very brittle and appear to have been actually formed in the abscess cavity. Now and then one meets with hard laminated and facetted calculi, which have the appearance of ordinary gall-stones. In such cases the concretions have usually made their way by perforation from the gall bladder, or from the trunk or chief branches of the hepatic duct. The pus from calculous abscesses of the liver has frequently been subjected to bacteriological investigation. Leyden, Rovighi, Brieger, Martha, and Netter have found streptococci in it. On the other hand E. Levy obtained pure cultures of *bacterium coli commune* in the case in my clinic above referred to. Yet this is in no way characteristic of hepatic abscess from calculus, for Veillon and Jeille have cultivated the same bacillus from the pus of a dysenteric abscess.

The condition of the blood-vessels of the liver in cases of calculous abscess is the same as with other varieties of hepatic abscess, *i.e.*, the afferent branches of the portal vein are often found thrombosed, and in a case of Joffroy's, with abscesses of the bile ducts, the hepatic artery was also the seat of thrombosis. Those branches of the hepatic vein which are involved also

frequently contain thrombi. The thrombosis may be entirely secondary, but in cholelithiasis abscesses may also originate from portal embolism.

Hepatic abscesses can be formed in several ways as the result of cholelithiasis :—

(a) An empyema of the gall bladder may burst into the liver. Several cases of this kind have been reported, and one of Aufrecht's, which will be referred to later, is of special interest.

(b) Purulent cholangitis of the intrahepatic bile ducts leads to ulceration of the mucous membrane, and the ulcerative process spreads from the duct - walls to the neighbouring parenchyma of the liver. Such ulcerative pericholangitis is not unfrequently met with in numerous spots in the same liver.

The bile ducts around which the suppuration occurs are often filled with inspissated pus, or more frequently still with dark-coloured pultaceous deposits of bilirubin-calcium.

(c) In the cases described by Schüppel's pupils (Teufel and Carl) under the name of hepatitis sequestrans, the process is an entirely different one. In these cases also the suppuration spreads from the smaller bile ducts, but instead of an extension of the infection from the ducts to the parenchyma of the liver, necrosis of the liver cells appears to have first taken place, in the periphery of the lobules, under the influence of the bile confined in the ducts, followed by a casting off of the necrosed tissue as the result of suppuration along its edges. Such a process is rendered quite intelligible by the results of Chambard, Beloussow, Steinhaus and Pick, who always observed such necrosis of liver cells, as a result of biliary obstruction, in experiments with ligature of the common duct.

(d) Lastly, hepatic abscesses occurring with cholelithiasis may be truly metastatic, i.e., embolic.

In a number of cases such a connection between the cholelithiasis and the hepatic abscesses is quite evident, pylephlebitis being set up by a calculus incarcerated in the common duct. This may happen in one of two ways :—In the first place the stone in the common duct (which in such cases usually lies below the junction of the hepatic and cystic ducts, that is to say, where the portal vein and choledochus cross each other) may directly compress the portal vein, and so lead to

the formation of a thrombus. Such cases have been described by Leudet, Geigel, and others. In a case of Donkin's the compression of the portal vein leading to thrombosis was due to several large calculi in the gall bladder. In a case of Klesser's, the stone which lay in the cystic duct compressed only a single branch of the portal vein, and this alone was thrombosed. In these cases, in which the compression of the portal vein by a calculus leads to thrombosis, the thrombus does not necessarily become purulent.

Two cases which came under my own observation, of which short notes are appended, illustrate this point :—

CASE XIX.—A woman, aged 50. Jaundice for 6 months ; vomiting a fortnight ; rapidly increasing swelling of the abdomen.

November 15*th*, 1865 : Very considerable ascites and extreme jaundice. Liver slightly swollen and somewhat tender ; spleen enlarged.

The ascites increased, and on December 3rd there was hæmatemesis and blood in the motions, and coma developed. Death occurred on December 4th.

Autopsy.—In the cystic duct, where it joined the common duct, was a stone as large as a hazel-nut, which pressed on the portal vein. In the portal vein was an adherent clot, almost completely filling its lumen, but showing no purulent change. The mucous membrane of the intestine and stomach exhibited hæmorrhagic areas, but was nowhere ulcerated. Spleen considerably enlarged. There was, moreover, carcinoma of the gall bladder with secondary nodules in the liver.

The second case was very similar. It was that of an elderly female who was taken into my ward at Königsberg with considerable ascites, and died a short time after admission. At the autopsy a hard gallstone as large as a nut was found in the common duct, a little below the mouth of the cystic duct. The portal vein was compressed by it and contained an adherent clot. I cannot say for certain whether there was an hepatic abscess, but, as far as my memory serves me, I feel sure that, in this case also, there was no purulent breaking down of this clot.

In another group of cases incarceration of stones in the common duct results in perforation of its walls, and thus leads to the formation of an abscess between the duct and the portal vein, which had set up pylephlebitis. To this group belong the cases recorded by Bristowe, Quénu, and Boussy, probably a case recorded by Grainger Steward, and others. Fiedler, too, observed a case of thrombosis of the portal vein associated with an impacted gall-stone in the common duct, but the connection

between the thrombosis and the impacted stone was not established.

In cases in which the thrombosis is fibrinous the results of acute portal obstruction may of course develop, as in my Case XIX. When the thrombus is purulent they appear to be absent, as in other cases of that nature. As far as I am aware, the injury which the wall of the portal vein suffers has in no instance given rise to hæmorrhage.

Some authors, such as Budd, and quite recently Geigel, have held the view that hepatic abscesses, associated with chole-lithiasis, originate with embolism, even when there is no portal thrombosis. Geigel states in support of the possibility of such causation, and not incorrectly I think, that the blood from the mucous membrane of the gall bladder and bile ducts enters the vena porta. When there is ulceration of the biliary mucous membrane, germs of infection can easily be conveyed to the liver from this situation.

In cases of cholelithiasis the diagnosis of hepatic abscess frequently presents great difficulties, owing to the fact that in biliary fever in connection with cholelithiasis a group of symptoms often present themselves which are extremely like those of abscess, even when no abscess is present as a com-plication. Moreover, it is not unfrequently almost impossible to distinguish clearly between abscess and new growth.

Simple biliary fever is almost always very remittent, and often exhibits long intermissions. The exacerbations occur at irregular intervals, and are often accompanied with severe rigors. During such febrile attacks the liver may become enlarged and tender.

These are just the symptoms which attend the development of an abscess. Since, however, there is usually a severe primary infection of the bile passages, preceding the develop-ment of a large abscess, the febrile disturbance is usually more marked, and the temperature rises to a higher point during the exacerbations (rigors) in cases in which abscesses form. The temperature frequently rises to 41° (106° F.) in such cases, whereas in simple biliary fever it does not as a rule rise above 40° (104° F.). Again, with an abscess the temperature is less likely to remain normal for days together, although such intermissions lasting for weeks have been observed in some cases.

These excessive fluctuations of temperature exacerbations up to 41° (106° F.), followed by remissions to subnormal levels 36°—35·5° (97°—96° F.), are characteristic of a grave infection.

In cases of uncomplicated biliary fever the enlargement of the spleen is usually less marked. It is undoubtedly the fact that in cases with hepatic abscess the loss of strength is, as a rule, much more conspicuous and rapid, and there often quickly develop, *i.e.*, in the course of days or weeks, the characteristic symptoms of severe sepsis.

The condition of the liver is, of course, very important. If, as may be the case in severe febrile cholelithiasis, it is neither painful nor at all tender, this is opposed to the diagnosis of abscess.

Yet a painful condition of the liver as a whole, with increased pain and swelling during the febrile exacerbations, and rigors, do not afford proof of the presence of an abscess, since these symptoms are, as has been already mentioned, quite commonly present when there is no abscess.

I will here relate a case of the kind in which there was certainly no abscess formation, and may also refer to what Osler says on this point :—

CASE XX.—Wife of an Oberförster, aged 27.

History.—The patient has been married 11 years. Her first child was born 6 years ago; her last in the February of the present year. Normal labour and puerperium. Since the end of April she has suffered from intolerable itching of the legs and lower part of the body. About 7 weeks ago she became yellow; at the same time the stools assumed a grey colour, and the urine showed a yellow foam. Then followed pains of great severity, lasting 3 or 4 days at a time, and the patient detected a tumour below the costal arch, on the right side of the abdomen. After taking Carlsbad salts she had diarrhœa; previously there had been constipation. The patient suffers from loss of appetite, and states that she has lost much flesh since her illness began.

Present condition.—The patient is a rather tall, strongly-built woman, fairly well nourished. There is quite superficial œdema of the lower extremities. The temperature normal, pulse and respirations are not unduly frequent. The sclerotics and the skin everywhere have a deep yellow colour. Lungs, heart, spleen, genital organs normal. Percussion shows a marked increase of the liver dulness, and on palpation the sharp edge of the organ can be grasped at about the level of the umbilicus. The surface feels smooth, and there is no tenderness. Gall bladder not palpable. The urine is free from albumen, and gives no bile-pigment reaction. The stools have a greyish white colour.

The febrile attacks recurred at quite irregular intervals during her stay in the hospital, as may be seen from the temperature chart. Each exacerbation was attended with a rigor, severe colic, and a transitory enlargement of the liver, which at such times was tender. The itching and jaundice persisted, but there was no increasing loss of strength. No gall-stones were found. On December 21st the patient left the hospital. Carlsbad Mühlbrunnen water, enemata, poultices, and narcotics were employed without effect.

On the other hand pain, either spontaneous or on pressure, in circumscribed portions of the liver is, as has been mentioned, an important sign; and it is particularly suggestive of suppuration when the circumscribed spot always becomes more painful during a rigor. This has been previously pointed out by other observers (Osler), and I can confirm the statement from my own experience.

Circumscribed tenderness in the region of the gall bladder is not, of course, any indication of hepatic abscess, but is very common in connection with the attacks of pain connected with cholelithiasis. Lastly, it is not necessary to dwell upon the diagnostic importance of fluctuating tumours upon the surface of the liver.

On the whole it is well in cases of cholelithiasis to be in no hurry to arrive at the diagnosis of hepatic abscess. The severity of the infection does not in itself afford any proof of the presence of this lesion. In connection with cholangitis and cholecystitis it was pointed out at length how these are capable in themselves of leading to the gravest and fatal general infection, and for the production of this result no actual suppurative inflammation is required, but it suffices that the bacillus of Escherich be

present in the bile. This is very frequently the case without such grave consequences, and very probably is at the bottom of every case of biliary fever.

It is well to regard all cases of biliary fever as serious, but provided that there is no abscess, the bacterial infection of the bile may be quickly got rid of when the flow of bile is restored, and recovery takes place. Case IV. affords an instance of an extremely severe infection of this kind, which ended in complete recovery after the stone was passed.

In cases in which suppurating new growths occur, it is simply impossible to decide whether the case is one of new growth or of abscess. I once had an hepatic abscess, as large as a fist, opened. The operation was satisfactorily performed, but the abscess did not heal, and at the autopsy it turned out that the cavity, which was still as large as a walnut, was situated in a large carcinomatous nodule which had undergone suppurative change in its centre. The liver contained numerous tumours from the size of a millet seed to that of an apple, which were almost all breaking down into pus. There was a primary ulcerated carcinoma of the stomach.

Such cases are apparently not very rare, and I have seen another of just the same kind :—

CASE XXI.—The patient, a man aged about 60, had frequently suffered with severe symptoms of cholelithiasis for about 17 years. He had gone through several courses at Carlsbad. For 6 weeks he had been feverish, with gradually rising temperature (38·7° (101·7° F.) in the morning, up to 40° (104° F.) in the evening). Jaundice for the last few weeks ; much loss of flesh ; deep jaundice. The liver, which was evenly enlarged, extends for several fingers' breadth below the costal arch. The border was nowhere irregular, except in the region of the gall bladder, where it was very tender on pressure. The diagnosis of carcinoma was made. A few days later pus was obtained by a surgeon by means of an exploratory puncture in the tender spot on the border of the liver. Laparotomy was performed, and a large carcinomatous nodule was found which had undergone softening in its centre.

The patient succumbed to the operation.

Even in cases of new growth without any suppuration, remittent and intermittent fever may be present, and even severe rigors. I have related such a case above (Case XII.).

4. *Ulcerative Affections of the Biliary Passages, and Fistula Formation.*

The changes undergone by the walls of the biliary passages in cholelithiasis are best studied in the gall bladder. If, owing to obstruction of the cystic duct, the emptying of the bladder is impeded for a long period, there results, according to Janowski and Orth, hypertrophy of its muscular coat. The hypertrophied muscular bundles may project, forming ridges and furrows upon the mucous surface, so that an appearance may be presented which recalls that exhibited by the urinary bladder when its muscular coat is hypertrophied (Orth). Sooner or later a desquamative catarrh develops, with thinning of the mucous membrane of the gall bladder, and very frequently there ensues an ulcerative affection of the mucous membrane. This is often met with just at the spots upon which the concretion exerts pressure, and must then be regarded as of mechanical origin. The ulcers may heal, and thus scars are formed such as are often met with on the mucous membrane of the gall bladder. Such scars are most often situated in the neck of the gall bladder, in the cystic duct, and at the duodenal end of the common duct, that is to say, in the situations in which calculi are usually incarcerated, and in which the mucous membrane suffers from their presence. Not uncommonly they lead to narrowing or even occlusion of the lumen ; thickening and fibrous degeneration of the walls of the bile ducts and gall bladder is quite a usual event ; and in several instances the wall of the gall bladder has been found extensively calcified.

A very remarkable effect which has been several times observed is the encapsulation of a calculus in the cavity of the gall bladder. Septa, either complete or incomplete, are developed from the inner surface of the cavity, separating the concretions with which it is filled, so that the gall bladder becomes converted into a number of fibrous capsules, more or less shut off from each other, in each of which one or more concretions lie. Extensive destruction of the wall of the gall bladder from ulceration may also result. Extensive phlegmonous infiltrations have also been met with, and the mucous membrane has been found undermined and necrosed.

Finally, inflammation of neighbouring structures may result,

directly or indirectly, from the ulceration, and thus perforations and fistulæ are formed. It is not usually the case that a primary perforation of the ulcerated wall of the bile passages occurs, but much more frequently there is an extension of the inflammatory process to the neighbouring parts, the wall remaining complete. This results in the formation of a pericholitic abscess and later on perforation from within outwards may readily occur, or even from without inwards, *i.e.*, from the secondary abscess into the cavity of the gall bladder or bile ducts. The sequelæ of such ulcerations and perforations of the biliary passages are various.

(*a*) *Hæmorrhage from the biliary passages; hæmorrhage into the stomach and intestine.*—Although strictly speaking only such intestinal hæmorrhages as are included under heading 4. should here be considered, it appears to me convenient to speak collectively at this point of the various forms of gastric and intestinal hæmorrhages which occur in connection with cholelithiasis. They are by no means rare, and they have various origins.

1. In long-standing severe jaundice a hæmorrhagic diathesis often ultimately develops, often with very abundant hæmorrhages from the mucous membrane of the stomach and intestines. Such is the termination of many cases of chronic gall-stone jaundice, and it has long been known how dangerous such hæmorrhages are. The danger is even greater when the patient passes into a state of coma or delirium simultaneously with, or shortly before or after, the onset of hæmatemesis or melæna— the well-known group of symptoms of the so-called cholæmia. Such cases are almost always fatal, although examples are known in which recovery has taken place.

2. Cholelithiasis can lead to intestinal hæmorrhage by causing portal thrombosis, as in Case XIX., which results from the intense congestive hyperæmia of the mucous membrane of the stomach and intestines. Capillary hæmorrhage into the gastric and intestinal mucous membrane and upon its surface may follow. Such hæmorrhages may be very copious in portal thrombosis, but I am not aware that they ever are so in cholelithiasis.

3. In cholelithiasis fistulæ are not unfrequently formed between the biliary passages and the stomach or intestine, and the ulcerative perforation of the gastric or intestinal wall occasionally gives rise to severe hæmorrhages. Hæmate-

mesis and severe and even fatal intestinal hæmorrhages have been repeatedly observed in such cases. Thus Rose saw an elderly woman die from the penetration of a large stone into the duodenum. I have myself seen the following case :—

CASE XXII.—A woman, aged 52, had frequently suffered from symptoms of cholelithiasis. At the end of May, 1889, there occurred a fresh attack of acute cramp-like pains in the hepatic region, with vomiting and rigors, followed by great loss of blood in the stools. The patient was in my wards in Strasburg from the 8th of July to the 15th of August, with symptoms which were equally compatible with circinoma of the pylorus or irregular cholelithiasis. At the autopsy there were found, in addition to other lesions, fistulæ between the gall bladder and both duodenum and colon. (This case has been already published by Schüller.)

Fiedler recorded the following case in 1880 :—

A woman, aged 66. She had suffered a year previously from an attack of acute gastralgic pain with a rigor. Then followed dilatation of the stomach, vomiting of blood-stained material, and transitory tumour at the pylorus, after the disappearance of which there was constipation for 6 days, ending with the passage of a large gall-stone (weighing 12 grammes).

Ross recorded an exactly similar case in 1885 :—

A man, aged 50, had long suffered from cholelithiasis, with frequent colic accompanied by jaundice. Hæmatemesis, quickly followed by the passage of a gall-stone weighing 16 grammes, after 6 days of intestinal obstruction with tympanitis and vomiting.

Boisson (Fauconneau-Dufresne, p. 264) described a case with repeated vomiting of blood, and later of black material and gallstones. Habershon observed repeated hæmatemesis in a case in which the autopsy showed that the blood came from a fistula between the gall bladder and duodenum.

I believe that, if more attention had been directed to this point, many cases of hitherto unexplained gastric and intestinal hæmorrhage would have found their explanation in the formation of biliary fistulæ. Cholelithiasis appears to frequently cause hæmorrhage from the biliary passages themselves. The best example of this is afforded by a case observed by A. Cahn :—

An elderly woman had long suffered from epigastric pain and vomiting after food. The diagnosis lay between round ulcer of the stomach or duodenum and cholelithiasis. No gall-stones could ever be found in the stools. Five weeks before her death there occurred a

copious gastric and intestinal hæmorrhage, and a few days later a more severe one, with the passage of bright red blood from the bowel. Then followed slight jaundice without discolouration of the stools, and this repeatedly recurred in a transitory manner. A similar hæmorrhage occurred 3 weeks before death, and finally a rapidly fatal intestinal hæmorrhage.

M. B. Schmidt found : False aneurism of the right hepatic artery, " which lay in contact with that part of the hepatic duct which was over against the point of a gall-stone which had penetrated into it from the cystic duct." This aneurism had ruptured into the hepatic duct. There were in addition three perforations from the gall bladder into the duodenum.

A few other cases of fatal hæmorrhage from the biliary passages have been observed. Chiari reports an almost similar one :—

A man, aged 33, had suffered for 4 weeks from attacks of gastralgia. After the passage of small quantities of blood *per anum* for a few days, he succumbed to a copious intestinal hæmorrhage. Chiari found three aneurisms of the cystic artery, the largest of which, (2 centimeters long by 1 centimeter across) had ruptured into the gall bladder. There was an old fistula between the gall bladder and duodenum.

Here also cholelithiasis was presumably the cause.

Lebert's case, too, appears to have been one of cholelithiasis.

It was that of a woman, aged 30, who died of hæmatemesis and melæna. Lebert found that an aneurism of the hepatic artery had burst into the gall bladder. There was also ulceration of the mucous membrane of the gall bladder.

In Aufrecht's case cholelithiasis acted, but in another way, as the undoubted cause of fatal hæmorrhage into the biliary passages. A large stone had partially broken through, from the gall bladder into the hepatic tissue. This led to severe hæmorrhage, and the blood had entered the gall bladder, and thence had flowed into the intestine along the cystic and common ducts. The patient, a man aged 46, had long suffered from cholelithiasis, and died of hæmatemesis. For the sake of completeness it may be mentioned that Quincke's case of aneurism of the hepatic artery, with intestinal hæmorrhage, and Pearson Irvine's case of hæmatemesis, due to the rupture of an aneurism of the hepatic artery into the stomach, do not appear to have had any connection with cholelithiasis.

(b) *Perforations and the formation of fistulæ.*—Perforation of the wall is most frequently met with in the gall bladder, but may also occur in the cystic or common duct. Adhesions to neighbouring organs have often been formed, or the perforation takes place in a previously formed pericholitic focus of inflammations. If this is not the case, the contents of the gall bladder, or of the duct, escape into the abdominal cavity. Peritonitis usually results, but even with cholecystitis the bile may be sterile; and it is therefore conceivable that such a perforation may occur without setting up inflammation of the peritoneum. A few cases have indeed been observed in which several litres of pure bile have been evacuated from the abdomen by puncture, and recovery has followed without peritonitis. This was the case in an example quoted by Harley (*l.c.*, p. 474), and in Erdmann's case, in which 60—80 pounds (*sic*) of bile were removed by puncture. However, these do not appear to have been cases of cholecystitis.

The peritonitis may at once become general and prove fatal, and this is what usually happens when the perforation follows upon an attack of colic (conf. p. 89). Under other circumstances it more frequently remains circumscribed, and an abscess around the gall bladder, or some such lesion, results, when one was not already in existence before the perforation. Such abscesses sometimes contain pure pus, sometimes bile, and even one or more gall-stones of greater or lesser size. They are usually concealed under the liver, lying between that organ and the stomach and great omentum. When they originate in the gall bladder they are usually situated behind the anterior abdominal wall, below the liver, or are subdiaphragmatic, lying upon the convexity of the liver. The symptoms of such pericholitic, *i.e.*, pericholecystitic, or pericholangitic, abscesses are almost always quite obscure, except in cases in which they originate from empyema of the gall bladder; and such foci of suppuration may produce grave effects by causing sepsis, even when they are beyond the reach of diagnosis. Their chief interest lies in the fact that they lead to the formation of the multiple fistulæ, soon to be described, when they burst into one of the neighbouring organs.

This is the usual outcome, and it much less commonly happens that an abscess near the gall bladder ultimately

bursts into the peritoneal cavity and causes peritonitis. Perforation of the gall bladder or duct-wall may, of course, lead directly to the formation of a fistula, as, for example, when adhesions have been already formed between the bile passages and a neighbouring organ. It is in this way, *i.e.*, without the intermediate formation of a pericholecystitic abscess, that fistulæ between the gall bladder and duodenum or colon, and especially those between the common duct and duodenum, not unfrequently originate. The following table affords information as to the varieties of fistulæ resulting from cholecystitis and their frequency (in recorded cases). It is chiefly taken from Courvoisier :—

FISTULÆ :—

Between the bile ducts themselves	... ...		8
Retroperitoneal	... ...		4
Gastric—total	... ...		12
Gastro-hepatic	...	4	
Between stomach and gall bladder	...	8	
Duodenal—total	... ...		108
Common duct and duodenum	... ...	15	
Gall bladder and duodenum	... ...	93	
Between gall bladder and jejunum	... ...		1
Between gall bladder and ileum	... ...		1
Colic—total	... ...		50
Between gall bladder and colon ...	...	49	
Between common duct and colon	...	1	
Urinary passages...	... ...		6
Thoracic viscera	... ...		10
Abdominal wall	... ...		184
			384

However, as Courvoisier himself correctly remarks, these statistics afford no correct notion of the actual frequency of the several varieties of fistulæ. Fistulæ of the abdominal wall appear in much greater numbers than are justified by their actual frequency, because they have always attracted particular attention. The same is true of fistulæ into the lungs and urinary passages, although they are so few in number in the above series. On the other hand, the most important fistulæ of all, the gastric and intestinal, in no way compel attention, and are generally only found on careful dissection. Fistulæ between the common duct and duodenum, which are perhaps the most

important of all, have doubtless been frequently misinterpreted, up to quite recent times.

A correct notion of the frequency of fistulæ in general, and of the individual varieties, may be obtained from the following statistics. The numbers are small, indeed, but they correctly conform to the indispensable rules of statistics. They are as follows:—

	Roth.	Schröder.	Schloth.	Total.
Total of autopsies	5,403	1,150	4,313	10,866
Gall-stones present in	535	151	343	1,029
Perforations into the perito-				
neum—total	—	1	2	3
(a) of gall bladder	—	—	2	2
(b) of cystic duct (rupture)...	—	1	—	1
Fistulæ—total	25	8	13	46
(a) between the several bile				
ducts	—	—	1	1
(b) between gall bladder and				
liver	—	—	1	1
(c) between gall bladder and				
stomach...	—	1	—	1
(d) between gall bladder and				
duodenum	12	1	6	19
(e) between gall bladder and				
colon	8	5	3	16
(f) between common duct				
and duodenum... ...	5	—	—	5

1. Fistulæ between the various bile passages have merely an anatomical interest.

2. Fistulæ into the portal vein have a somewhat wider interest, seeing that the penetration of gall-stones into the portal vein always leads to pylephlebitis and portal thrombosis. Their relation to cholelithiasis has been considered already in connection with suppurative hepatitis.

I have found three cases in all of penetration of gall-stones into the portal vein,* which are severally recorded by Deway, Murchison, and Roth. In all three cases there were periphlebitic biliary abscesses, originating from the common duct, with erosion of the wall of the vein and pylephlebitis. The symptoms showed nothing of special interest during life, and the symptoms of portal thrombosis were absent.

* Courvoisier includes a fourth case (of Bristowe's), bnt I cannot see that in this instance there was penetration of a stone into the portal vein. It merely presented a periphlebitic biliary abscess and pylephlebitis.

3. Retroperitoneal fistulæ are remarkably uncommon. In the three cases which Courvoisier records they originated from perforation of the gall bladder. I have observed one case in my wards at Königsberg:—

CASE XXIII.—The patient, a woman aged 60, was admitted with jaundice and ascites, and died, in hospital, in a few days. At the autopsy a large gall-stone was found in the common duct just above the *portio duodenalis*. The duct was much dilated, and showed a large perforation. Through this opening one came into a sack filled with a sediment of bilirubin-calcium and with pus, which was connected with a biliary-purulent infiltration of the retroperitoneal tissue. This extended downwards and outwards, behind the ascending colon, as far as the iliac fossa (the vermiform appendix being free), and towards the middle line as far as the ascending vena cava, the wall of which was perforated, and in which lay a soft thrombus. In the vein, as in the retroperitoneal infiltrations, were yellow brittle masses, which were apparently deposits of bilirubin-calcium.

4. Fistulæ between the urinary and biliary passages are extremely rare. Courvoisier collected five undoubted cases, in all of which the stones were passed, whilst in that of Güterbock lithotrity was resorted to. J. P. Frank has described the passage of a stone through the vagina, but in all probability there was no actual biliary-vaginal fistula.

5. Cholelithiasis is not the predominant cause of biliary-thoracic fistulæ, which more frequently owe their origin to suppurating hydatids than to gall-stones. The perforation does not usually take place directly from the bile passages in such cases, but it did so in Cayley's case, from a dilated bile duct on the convexity of the left lobe of the liver; and also in a case recorded by Mandard. In this latter the fundus of the gall bladder itself had become adherent to the under surface of the diaphragm, and had perforated into the lung direct. The cavity of the gall bladder formed with the pulmonary abscess a large "cloaca," in which numerous gall-stones were present.

More frequently the perforation follows upon a calculous hepatic abscess, or upon a pericholicystitic abscess beneath the diaphragm. Rupture may occur directly into the lung (when pleural adhesions have been previously formed), and then pulmonary abscess usually results; or it may take place into the pleural cavity, causing empyema or pyopneumothorax, with ultimate rupture into the lung, if the patient survives long

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enough. In Pasturaud's case there existed a *pyopneumothorax subphrenicus,* which had ruptured into the right lung, and Hippocratic succussion was present. Naturally it is almost always the right lung or pleura into which rupture occurs.

In two cases (Courvoisier) rupture into the left pleura occurred. In one case (Simons) the abscess first burst into the mediastinum, and later perforated into the main bronchus. I know of only one case in which perforation into the pericardium resulted.

The fluid in the pleura and pericardium has usually contained more or less purulent bile. Harley, in one instance, found the penetrating gall-stones in the pleural effusion. As a rule, but not always, bile has been expelled in large quantity with the sputum in such cases. Calculi never appear to be thus expelled. Biliary-thoracic fistulæ appear to have all been fatal with a single exception (Riedel).

6. Biliary fistulæ of the abdominal wall are of greater practical importance. They almost always originate in the gall bladder, and, as a rule, owe their origin to empyema of that viscus. However, the ultimate external rupture does not by any means always occur in the right hypochondrium, but may have its seat in the right mesogastrium or hypogastrium, or even in the left side of the abdomen. The commonest place, indeed, is at, or in the immediate neighbourhood of, the navel. The reason why the rupture at the navel is so remarkably frequent lies, according to Richtet's very instructive explanation in the "*trajet ombilical,*" which he describes. This umbilical channel, which may be compared to the inguinal canal, runs in the anterior abdominal wall from the point of entry of the (obliterated) umbilical vein to the navel, having a length of 3—6 cm. ($1\frac{1}{4}$—$2\frac{3}{8}$ in.). Along this track pericholecystitic lesions, originating near the gall bladder, and attacking the inner surface of the abdominal wall, can easily extend to the umbilicus.

The origin of the inflammatory condition which ultimately results in rupture is not infrequently attributed by the patient to an injury, such as a blow, pressure, or squeezing in some uncomfortable position, and the like. In some instances the impetus to rupture appears to have been imparted by an acute febrile disease.

In the great majority of cases symptoms of cholelithiasis have

been previously present, and in only a few do they appear to have been wanting. In a considerable number of cases only pus, or viscid fluid (contents of the gall bladder), but no bile has been evacuated. In such instances the cystic duct has often been obliterated.

If the cystic duct be patent, bile flows from the fistula, at least occasionally, and even apart from closure of the common duct, a permanent complete biliary fistula may result, that is to say, the whole of the bile may escape through the fistula in spite of the fact that the common duct is patent. Hertz's excellent case illustrates this. In this instance the whole of the bile (532 cc. (18 oz.) in the 24 hours) escaped externally as long as the fistula remained open, for the motions were completely devoid of bile; but a few days after the fistula was got to close the motions had resumed their normal colour. There was never any jaundice.

The fistulous passages are, as Frerichs pointed out, usually narrow and tortuous, and offer considerable impediments to the passage of the bile; and consequently the amounts of bile voided through natural fistulæ are seldom comparable with those obtained by cholecystotomy. However, the amount of the flow is often sufficient to be extremely inconvenient.

In a considerable number of cases, and not only in recent ones, gall bladder fistulæ have been got to heal by means of suitable operative procedures, and often after the passage or removal of stones. The calculi have sometimes been passed by hundreds, the individual stones being occasionally as large as a hen's egg, or even larger. When the fistula has reopened at a later period it has often been found that another stone was making its way outwards. Jaundice has only been present in the minority of instances. In a few cases it has disappeared after the expulsion or removal of the calculus, as in one observed by Saureau (Fauconneau-Dufresne, p. 306). As a rule it has been due to a closure of the common duct as a complication, and has not disappeared in spite of the formation of the fistula. When natural fistulæ have existed for years they are not usually well borne. The patients fail, and in the end tuberculosis of the lungs frequently develops. This appears to be the commonest immediate cause of death in cases in which the patient does not succumb in some manner to jaundice.

The actual cause of the exhaustion of the patients is no doubt suppuration in the fistulous passages, but formerly it was believed that the loss of bile through the fistula was very dangerous. The "säfteverlust" was dreaded, and still more the disturbance of the digestive functions resulting from the absence of bile from the intestine. This fear, which was based on the statements of Bidder and Schmidt, has been made too much of.

The more recent investigations of Röhmann and others have shown that intestinal digestion is but little disturbed by the absence of bile ; but numerous observations on human beings teach us that the loss of large quantities and even the whole of the bile through an external opening is well borne, even for a long period. Kendal Franks records a case illustrating this ; and in Harley's case (l.c., p. 401) the patient enjoyed perfect health in spite of an enormous loss of bile (270 grammes daily). He died at the age of 74, after the fistula had existed for 8 years.

7. *The formation of fistulæ between the biliary passages and the intestinal tract.*—These are by far the commonest of biliary fistulæ. The table given on p. 144, compiled from the statistics of Roth, Schröder, and Schloth, leaves no doubt on this point. Such fistulæ originate from almost any section of the biliary apparatus, the liver, gall bladder, and cystic or common duct ; but I have been unable to find any example of a fistula between the hepatic duct and the stomach or intestine. As a matter of fact they almost always have their starting-point in the gall bladder, but duodenal fistulæ sometimes start from the common duct. Perforation may take place into any part of the intestine, and it is not uncommon for perforations to occur in two distinct situations, with the result that a combined biliary-gastric-duodenal, or (more commonly) a biliary-duodenal-colic fistula is formed.

Cases of fistulæ opening into the small intestine are quite exceptional, no doubt on account of the great mobility of this portion of the bowel. Courvoisier quotes a case of fistula opening into the ileum, recorded by Wising ; and I have come across one of fistula between the gall bladder and jejunum, reported by Gaston, if indeed I rightly understand his description.

Biliary-gastric fistulæ are comparatively rare ; not more than

a dozen appear to be on record. Their gastric end is apparently always in the neighbourhood of the pylorus, and consists of one or more orifices. In one case the fistula started from an hepatic abscess, in one from dilated intrahepatic ducts, in one from the cystic duct, and in the remaining cases from the gall bladder.

Duodenal and colic fistulæ are alone important on account of their frequency. Gall-bladder-duodenal fistulæ appear to be the commonest. On this point the two different series of statistics given on pp. 143 and 144 are in complete accord ; however, as we shall be once more obliged to insist, one variety of duodenal fistula has hitherto been frequently overlooked. I allude to the fact that as a seat of origin of duodenal fistulæ the common duct may contest with the gall bladder the foremost place. From the statistics, and even from those of Roth, gall-bladder-duodenal fistulæ appear to be much commoner than choledocho-duodenal. Yet Roth's own valuable investigations have shown how easily choledocho-duodenal fistulæ may be misinterpreted, and on this point even the earlier observations of Roth himself cannot be regarded as free from the doubt, thus inspired, as to the adequacy of the older post-mortem records. Roth has shown that in cases in which a conspicuous widening of the *ostium duodenale* is stated to have been met with, but in which such dilatation was not established by examination of the papilla, the existence of a choledocho-duodenal fistula should be suspected. If this be granted, such fistulæ are, as far as my knowledge of the literature extends, hardly less common than those of the gall-bladder-duodenal variety.

Choledocho-duodenal fistulæ occupy a peculiar position in two not unimportant practical aspects. In the first place they are almost without exception produced in a much simpler way than any other biliary fistulæ. A calculus in the common duct, which is too large to pass through the *portio duodenalis*, and therefore remains fixed in the duct above that situation, causes a simple mechanical perforation of the wall of the duodenum. As a matter of fact, the orifice presents itself almost invariably as a direct opening leading from the choledochus to the duodenum, without any fistulous passage. It is only in quite exceptional cases that the calculus perforates the duct-wall higher up, and the resulting abscess about the choledochus ruptures in turn into the duodenum. Moreover, after the

expulsion of the stone, the parts may present a nearly normal appearance, whereas other fistulæ, such as those between the gall bladder and duodenum or colon are less favourable; the fistular passages, which are often long, are in themselves not so free from risk, and by their very existence introduce 'dangers of many kinds.

According to Courvoisier, perforations of the wall of the gall bladder are usually situated in the fundus. In fistulæ between the gall bladder and duodenum this is so in five-sixths of the cases, whilst fistulæ into the colon almost invariably occupy this situation, few exceptions being met with.

Cicatrisation of fistulæ appears to be uncommon. Schloth among his forty-three cases with gall-stones met with fourteen with "radiating scars, which were intimately related with fistula formation"; but Roth only saw a single cicatrised fistula among 535 cases with gall-stones.

It is in many cases possible to make the diagnosis of biliary, gastric, or duodenal fistulæ, provided that the formation of the fistula takes place under the eyes of the observer; but the course differs entirely in different cases. In many cases the jaundice, due to the calculi, which had become chronic, takes a most favourable turn and rapidly disappears, simultaneously with the expulsion of stone of such a size that it could only have escaped through a fistulous opening. In such cases it is probable that a choledocho-duodenal fistula has been formed. Such an example is recorded as Case X. Again, in cases of chronic jaundice of this kind the jaundice may diminish or disappear together with its effects; the fæces may become permanently bile-stained, although the pains or rigors persist; under these circumstances a fistula may have formed, but the stone may not have escaped. Aufrecht has published such a case with the autopsy. Cases such as the following, taken from the practice of a colleague, are the most accessible to diagnosis :—

CASE XXIV.—In this there had been no symptoms of colic until an inflammatory hardness developed in the right hypochondrium, which quickly disappeared. A few days later there followed pains in the ileo-cœcal region, with a hardness and symptoms of intestinal obstruction. The diagnosis, made by the physician, of calculus, escaped from the biliary passages and lodged in the *valvula Bauhini*, was quickly confirmed by the passage of a stone stated to have been as large as a nut.

Still other appearances were presented in the cases of Fiedler and Ross already referred to, viz., gastric disturbance, signs of dilatation of the stomach, hæmatemesis, temporary appearance of a pyloric tumour, symptoms of intestinal obstruction lasting 6 days, and passage of a large calculus.

Hæmorrhage accompanying the formation of a fistula will probably, when carefully looked for, prove to be more common than has been hitherto supposed.   Jaundice cannot be reckoned upon, since the fistulæ start from the gall bladder in certainly more than half the cases.

5. *Intestinal Lesions due to Gall-stones.*

Obstruction of the intestine by gall-stones may occur at any part from the pylorus down to the anus.   In this connection a quite peculiar place is occupied by—

(*a*) *Pyloric stenosis due to gall-stones.*—Cases are described by Pepper, Miles, Fiedler, Ross, Hale White, and Ogle, in which stenosis of the pylorus resulted from gall-stones.   In all the cases dilatation of the stomach resulted, and in Miles's case, and in that related below, from my clinic in Königsberg, there was active fermentation of the gastric contents.   In Fiedler and Ross's case there was hæmatemesis, and the gall-stone, pressing upon the pylorus, was palpable as a tumour.   Indeed, in all the cases the diagnosis of carcinoma of the stomach appears to have been made.   In Case XXV. also, which I observed in Königsberg, and which Minkowski has already briefly referred to, the same diagnosis was arrived at :—

CASE XXV.—Man, aged 57.

History.—Never any biliary colic or jaundice.   A year and three-quarters ago the patient noticed a hard tumour in the right hypochondrium, which quickly attained the dimensions of a hen's egg, and afterwards gradually diminished in size after it had been present for about 7 months.   Simultaneously with the appearance of the tumour, there occurred frequent and almost daily vomiting of material which was not blood-stained.   The vomiting ceased again for a time, and the gastric disturbance diminished.

For the past year there has again been frequent vomiting, eructations, and a dull ache in the right epigastrium.   The patient's nutrition has suffered severely.

He is a very cachectic and extremely emaciated man.   Jaundice is absent.   The stomach is enormously dilated, and when distended by

means of an effervescent powder, produces great bulging of the meso-
and hypogastrium.   Over the swelling active peristaltic movements
proceed in broad waves from left to right.   The stomach rests upon
the *symphysis pubis,* is always over-filled, and contains fermenting
masses (torulæ and sarcinæ).   Washing out relieved the symptoms,
and the stomach shrank upwards, but the fermentation continued.
At the beginning of December a tumour was first distinctly felt at
the pylorus.   On December 12th coma suddenly developed, with
stertorous breathing, and the patient remained in the same condition
up to his death on December 16th.

Post-mortem notes : The greater curvature of the stomach reached to
a hand's breadth below the thoracic wall.   The liver extended about two
or three fingers' breadth below the thoracic wall.   In the region of the
gall bladder there projected a tumour of stony hardness, about as large
as a goose's egg, which was in part adherent to the pyloric region of
the stomach, and in part to the right flexure of the colon.   After
opening the stomach along its greater curvature, and on attempting to
pass a finger through the pylorus, one noticed a tumour pressing down-
wards into the concavity of the stomach, which greatly interfered with
the patency of the pyloric opening.

After the removal of the stomach, together with the liver and
adherent portion of the colon, and after the stomach and duodenum
had been completely opened up, an opening as large as a halfpenny was
seen in the wall of the duodenum just below the pylorus ; a probe
passed through, which encountered a hard resisting substance.   This
on closer investigation proved to be a cholesterin calculus about the size
of a goose's egg, lying in the gall bladder, and completely filling the
cavity of that viscus, which was somewhat dilated and thickened and
ulcerated all over its inner surface.   In addition to the communication
with the stomach, there was a further ulcerative communication between
the gall bladder and the hepatic flexure of the colon.   There were, more-
over, a few other ulcerative orifices in the gall bladder, some of which
led into the duodenum, and others into the hepatic flexure of the
colon.

In 1889 Schreiber had under treatment in Königsberg a
woman, aged 29, who had suffered for 6 months with great
dilatation of the stomach and excessive wasting.   Stenosis of
the pylorus from simple ulcer was diagnosed, and an operation
was proposed.   After opening the stomach Mikulicz found at
the base of the pyloric ulcer a gall-stone larger than a thumb-
joint.   This was extracted, and the patient's recovery was
complete and permanent.   (Reported by Professor Schreiber.)

In Miles's case recovery took place after the vomiting of two
large gall-stones, whilst Fiedler and Ross's patient recovered
after the passage of the stone *per anum.*

In all the cases which terminated fatally the pylorus was compressed by gall-stones. These lay either in the gall bladder which had become adherent, or between the gall bladder and pylorus, in a pericystitic cavity. Fistulæ were also present, opening either into the stomach or duodenum, usually into both.

The thickening and cicatricial traction which the pylorus underwent as a result of this fistulous process contributed to its narrowing. In Mader's case, for example, the stone itself does not appear to have been the cause of the occlusion of the pylorus.

(b) *Intestinal obstruction by gall-stones.*—Calculi which are not conspicuously bigger than a large pea, or at the most as large as a hazel-nut, can alone reach the bowel *per vias naturales*. Larger ones can only be expelled from the biliary passages through fistulous openings. Such large calculi may lead to disturbances of various kinds in the alimentary canal, and especially to intestinal obstruction. Since, however, fistula formation occasionally takes place without pain or disturbance, there results an apparent paradox, viz., that whereas small stones pass *per vias naturales* into the intestine and usually with severe symptoms, but when once there are harmless and are expelled unnoticed; larger ones, the presence of which in the bowel may easily be attended with danger, often produce no symptoms in getting there. Even large calculi may pass along the bowel without serious difficulty. Blackburne saw a stone of the very largest size expelled *per anum* without any marked intestinal symptoms, and at any rate without causing obstruction. This stone measured 4 cm. ($1\frac{9}{16}$ in.) in its shortest, and 9·5 cm. ($3\frac{9}{16}$ in.) in its longest diameter.

A patient of Ord's passed a stone of 4 cm. ($1\frac{9}{16}$ in.) shortest, and 5 cm. (circ. 2 in.) longest diameter a fortnight after her delivery, with but little ill-defined disturbance.

Goldschmidt (of Strasburg) had under his care for some years a lady, aged 31, with cholelithiasis and dyspepsia, who ultimately passed in a motion, without any special symptoms, a cholesterin calculus 5 cm. (2 in.) in length by 3 cm. ($1\frac{3}{16}$ in.) in breadth, and weighing 16 grammes. I myself have a specimen, larger than a pigeon's egg, measuring 3·5 by 2·5 cm. ($1\frac{3}{4}$ by 1 in.), which passed after severe biliary colic, but apart

from any indications of obstruction.   However, the number of stones having a minimum diameter of more than 3 cm. ($1\frac{1}{4}$ in.) which pass without producing obstruction is undoubtedly very small.

In three cases the agglomeration of smaller calculi has been the cause of obstruction.   In a case recorded by Puyroyer the stones appear to have become welded together in the intestine, whereas in the cases of Bermond and of Kraus, on the other hand, the conglomerate stones had apparently been formed in the gall bladder.   Such large calculi as are here in question almost always came from the gall bladder, and only in seven out of thirty-six cases (Courvoisier) did they come from the common duct.   The danger is greatest when they enter the intestine from a gall-bladder-duodenal fistula, since when they pass through a colic fistula, thus entering directly into the large intestine, the most dangerous part of their route is avoided, viz., the small intestine and, above all, the ileo-cæcal valve.

In ten out of seventy-five cases* in which the position of the stone in the intestine could be determined with sufficient accuracy it lay at the valve or a few centimeters above it.   In thirteen others it was within a mètre above the valve, whilst in only six cases did it lie in the large intestine (colon, sigmoid flexure, or rectum).   The greater danger connected with a calculus in the small intestine is also shown by the following figures :—

In thirty cases of fatal obstruction from gall-stones, the position of the fistula by which the calculus entered the bowel was stated ; in twenty-eight the duodenum, and in two the colon was the place of entry.   In its passage along the intestine the stone may be arrested in several parts, and at each spot where it rests it may produce more or less complete occlusion of the bowel.   During the intervals the lumen may be temporarily patent.   Moreover, the concretion may set up ulceration of the intestinal mucous membrane in each spot, from which perforation of the wall and consequent peritonitis may result.   Like irregular cholelithiasis in general, intestinal obstruction from gall-stones is specially apt to occur in elderly women.

* For the following numerical statements I have availed myself, after careful verification, of the material which Schüller has collected in his thesis.

Among 127 cases there were only thirty-four in men. The
ages of the patients of both sexes were as follows:—

Under 30 years	5
Between 31 and 40 years	7
„ 41 „ 50 „	26
„ 51 „ 60 „	45
„ 61 „ 70 „	25
Over 70 years	12

In the majority of cases there had been, at an earlier period,
undoubted symptoms of cholelithiasis. In twenty-six out of
forty cases, in which this point was referred to in the histories,
gall-stone colic, or pains referable to this cause, were mentioned,
and in eight only was it stated that these symptoms had never
been present. On the other hand, jaundice only occurred in
sixteen cases (out of forty-two in which this point was clearly
referred to), and in twenty-six others it was expressly stated
that there had never been any jaundice. This is easy to under-
stand, seeing that the large calculi with which we are here
dealing have seldom traversed the common duct, but far more
frequently have reached the intestine through fistulæ of the
gall bladder. In forty-one cases (out of about 120 available)
the development of the obstruction was immediately preceded
by symptoms which could be referred to the breaking through
of the calculus into the intestine. The history of previous
undoubted cholelithiasis naturally very much facilitates the
diagnosis ; but even apart from this the clinical picture may
be quite characteristic. As a rule vomiting soon sets in,
and fæcal vomiting is very common, having been noted in
seventy-seven ·out of 120 cases. Acute pain is also usually
present from the first. In the painful locality the circum-
scribed hardness of tumour may be felt, and usually the
pain and hardness of tumour change their situation in course
of the affection, and for a time at least become fixed in
the right hypogastrium. The obstruction of the intestine is
frequently incomplete or not lasting. Motions are passed from
time to time, sometimes even when fæcal vomiting is present.
Or the intestine may be patent for days or even for a week at
a time, and may then become obstructed afresh. Moreover,
it seems to me that the bowel is not, as a rule, impassable
for gases.

In the case which is fully described below, and which I myself carefully observed, I was all along confronted by the paradox that the patient had fæcal vomiting, whilst she continuously passed flatus, and other observers have noticed a similar condition. Thus in Maclagan's second case there was complete obstruction for 8 days, but flatus continued to be passed. In obstruction from other causes this is extremely rare. Tympanites, too, appears to be but little marked in the majority of cases, and in a number of instances this is remarked upon by the observers. Nevertheless it is often enough expressly stated that the bowel was completely obstructed for long periods, such as 16, 17, 26, or 28 days.

In a few instances the calculus has been found in the rectum and extracted. In other cases it could be felt *per rectum* in coils of intestine lying above it. When the position of the stone cannot be ascertained by palpation, it is usually very difficult to determine the seat of obstruction. When this is very high up copious vomiting of bile is an important aid to diagnosis. Cahn observed this in senosis of the duodenum, and I find this symptom mentioned in a case of Pye-Smith's, in which the patient vomited 5 litres (nearly 8½ pints) of bilious fluid in the course of 48 hours, and the stone lay 90 cm. (35½ in.) below the pylorus. I will here relate a case which presented an excellent picture of obstruction by a gall-stone :—

CASE XXVI.—Woman, aged 75. Admitted January 23rd, 1890. Died February 3rd, 1890.

History.—Has had fifteen children, of whom three are living. Has had no illness ; syphilis is denied. Four years ago the patient is said to have suffered from "spasm of the womb." The pains were situated in the lower part of the body, and had the same character as her present ones. The present illness commenced on Jan. 19th, 1890, with abdominal pain. The bowels were open after an aperient. Her condition then got worse, the abdominal pains increased, especially in the lower parts, and she was therefore warded. Condition on Jan. 24th : Abdomen somewhat distended, but not very tense ; no tenderness on pressure in any part. No definite tumour felt. Slight resistance in the left inguinal region above Poupart's ligament. Peristaltic movements of the intestine not visible. Dulness extending to a hand's breadth above the symphysis and into both sides of the epigastrium. No free ascites. Pulse feeble, irregular, and intermittent ; arteries atheromatous. Lungs and heart normal. On Jan. 25th, in the morning, the stomach was washed out ; the contents had a distinct fæcal odour. Four large enemata were given, two each day, with 5 drops of tincture of opium. A

little flatus passed, and the last enema brought away some fæcal matter. Urine contains much indol. On Jan. 26th condition unaltered. Patient very exhausted. On Jan. 27th a hard tumour as large as a child's head was clearly felt through the abdominal wall in the right iliac fossa. It was palpable bimanually from the rectum, and also from the vagina. It was tender on deep pressure. The intestine was washed out daily. During the night of 28th—29th a loose stool was passed, and there was scanty fæcal vomiting. On Jan. 29th four loose motions were passed spontaneously with flatus ; much indol in the urine. On Jan. 30th a large injection, followed by three stools, and by others during the afternoon and night. On Jan. 31st the patient was much collapsed, unconscious, and passed motions under her. Distension of abdomen slight, and limited to the right hypochondrium. On irritation of the intestine, peristaltic waves were produced. The tumour on the left side appeared somewhat smaller, and was very painful on pressure. Feb. 1st, three or four loose motions passed into the bed. Temperature 36° (96·8° F.). Patient very weak; pulse hardly felt. Abdomen lax, and no longer distended. Coldness of nose and extremities ; much indol in the urine. Feb. 2nd, collapse greatly increased, pap-like stools passed into the bed. Pulse almost imperceptible. Patient lies in an apathetic condition, does not answer questions, and sleeps continuously. Indol present. Death occurred during the morning of Feb. 3rd.

Autopsy on Feb. 4th, 1890 : Muscular system poorly developed; thick fat cushions, especially on the abdomen. The omentum, loaded with fat, covers the whole of the small and large intestines. No fluid in the abdomen. Stomach and liver normal. The edge of the omentum adherent on the left in the iliac fossa, and also above, in the lumbar region. When the omentum was slightly torn in the lumbar region a fæcal stinking fluid escaped. There then was opened on left side, in a second spot in the inguinal fold 5 centimeters from the symphysis, a cavity from which a slightly greenish ropy fluid, with a fæcal odour, was evacuated, and this abscess cavity constituted as a matter of fact a portion of the peritoneal cavity, enclosed by coils of small intestine. These were matted together and adhered to the anterior pelvic wall by soft adhesions. The affected coils of intestine were in parts reddened and in parts black in colour, and were covered in places with lymph. Outside this focus, at the symphysis, there was another encapsuled collection of pus, in which there were present, in addition to whitish pus, black masses and small yellow lumps. This cavity was bounded behind by a coil of small intestine, and above by the border of the omentum. This last coil, which formed part of the jejunum, could be traced upwards alongside the splenic flexure of the colon, and was adherent to the *appendices epiploicæ*, and here was an opening from which came the fæculant fluid referred to. Here there was a cross tear in the intestinal wall, with ragged edges, and into which the little finger could be introduced. Four cm. ($1\frac{9}{16}$ in.) from the first tear was a second in the posterior wall of the intestine and reaching as far as the insertion of the mesentery. Its margin was fairly smooth, indented,

but showing no other change. This latter orifice lay 45 cm. (17¼ in.) below the commencement of the jejunum. On the pyloric side of the chief opening, and at a distance of 5 cm. (2 in.) from it, was a small perforation which admitted a thick probe. Cæcum normal. Transverse colon much contracted, and containing a small quantity of slimy fæces. In its wall, at the point where it was adherent to the gall bladder, was a funnel-shaped blackish depression, and at the end of the funnel was an orifice through which a probe could be passed into the gall bladder. From the depth of the opening a large fæcal shred, followed by pus, was evacuated, and then one came against gall-stones. In the duodenum and stomach was some grey mucus with hardly any yellow tint. The duodenum was tightly dragged against the gall bladder. Four centimeters below the pylorus was an opening through which the little finger passed direct into the cavity corresponding to the gall bladder. From it there escaped brown turbid bile. The liver was small and the bile ducts were much dilated.

On distending the jejunum, below the above-mentioned perforations, several other perforations appeared close to the insertion of the mesentery. In the mesentery of the perforated coil, near the chief orifice, was a slit 2 centimeters long. No old adhesions were present. The intestines throughout contained masses of greasy fæces. In the ascending colon, 12 centimeters above the valve, was a lipomatous polypus of the mucous membrane of the size of a cherry. The mucous membrane of the ascending and transvere colons and of the sigmoid flexure was deeply reddened. A hard substance was felt in the rectum, and on cutting it open a free gall-stone was found, of oval form, 55 mm. (2$\frac{3}{16}$ in.) in length and 27 mm. (1$\frac{1}{16}$ in.) in diameter. At its upper end it was expanded, so that in that part its diameter was 30 mm.(1$\frac{3}{16}$ in.). It was brown in colour, smooth, and had no processes. No other changes were found in the rectum.

The duration of the obstruction varies greatly in cases which recover the condition and seldom lasts for longer than 10 days. Thus the duration in twenty-four such cases was—

In 1 case ...	...	...	...	...		30 hours.
„ 8 cases ...	...	...	...	from	2— 5 days.
„ 10 „ ...	...	...	...	„	6—10	„
„ 2 „ ...	...	...	...	„	11—15	„
„ 1 case ...	...	...	...	...	15	„
„ 1 „ ...	...	...	...	...	17	„
„ 1 „ ...	...	...	...	...	3 weeks.

Among cases ending in recovery the longest duration has been 28 days, in a case of Sand's which I find quoted by Treves (p. 331).

Nor are the fatal cases usually distinguished by any specially

long duration. Death ensued in thirty-three cases, which were
not operated upon, at the following periods :—

In	7 cases ...	...	...	...	from	1— 5 days.
,, 16	,, ...	...	...	...	,,	6—10 ,,
,, 6	,, ...	...	...	...	,,	11—15 ,,
,, 1 case	...	...	...	...	after	16 ,,
,, 1	,, ...	...	...	...	,,	18 ,,
,, 1	,, ...	...	...	...	,,	26 ,,
,, 1	,, ...	...	...	...	,,	28 ,,

In many cases the patients describe a more or less distinctly
localised sensation felt at the moment when the impacted
calculus is set free. In four cases recorded by Mayo, Marotte,
Martin and Watson (quoted by Schüller) the patency of the
intestine appears to have been restored by palpation for the
purpose of examination, or by massage; and in two of these
the patients themselves noticed this.

In cases of obstruction by gall-stones it frequently happens,
more frequently indeed than with obstruction of other kinds,
that the patient dies even although the patency of the intestine
is restored. The cause of the fatal result is usually perforation
of the intestine, and peritonitis which, as has been already
mentioned, plays an exceptionally important part in these cases.
This was the course of events in the case reported (Case XXVI.).
Moreover, the obstruction may be relieved prior to the passage
of the stone. In quite a number of cases several days or even
weeks pass, after the obstruction has come to an end, before the
calculus appears in the motion, or the stone may even be found
in the intestine *post-mortem* long after the obstruction has
ceased.

True relapses, in which, soon after the passage of a stone
causing obstruction, a second becomes impacted with a like
result, are extremely rare. I have only found one case of the
kind, which is recorded by Dessauer. Maclagan so interprets
two cases observed by him, but incorrectly I think.

Schüller's statistics show a higher mortality than those of
Courvoisier. Excluding the operation cases, there are in
Schüller's series eighty-two cases in which intestinal obstruction
was present; of these forty-six, or 56 per cent., were fatal.
Dufourt obtained just the same percentage of fatal cases (56 per
cent.), *i.e.*, of seventy-three cases of obstruction from gall-stones,

forty-one proved fatal, whereas Courvoisier only obtained a mor-
tality of 44 per cent. in a total of 125 cases. Since his statistics
are the most comprehensive, we may without hesitation accept
his encouraging conclusion. I have only included cases with
obstruction of a more severe type.

(c) *The calculus may cause lesions of the intestine in its passage,
without obstructing its lumen.*—It has happened that a gall-stone
has made its way into the vermiform appendix, the result of
which accident may be perityphlitis and fatal peritonitis. This
was the termination of a case briefly referred to by Budd (p. 326).
Schüller also quotes such a case of Trousseau's, and another
of Wegeler's mentioned by Fauconneau-Dufresne (p. 277).
I have, however, searched in vain for Trousseau's case ; and
in Wegeler's case he concretion, as was clear from its appear-
ance and chemical analysis, certainly consisted of fæcal material,
and was no gall-stone.

On the other hand, there is a case recorded (by Serey) in
which a gall-stone was expelled from an abscess, probably peri-
typhlitic, after rupture externally ; and a case of Rehn's, ending
in recovery, in which a calculus was removed at an operation
from an abscess in the neighbourhood of the cæcum.

A case quoted by Treves also (the source of which he does
not state) was probably of this kind :—

In the case of a child, aged 10 years, who had long suffered from
indigestion and bilious vomiting, a cholesterin stone as large as a pea,
and enveloped in fæcal material, was removed from an abscess to the
right of the spine. Recovery followed.

There are again a few cases in which a large calculus
clearly remained for a long time in the bowel, and caused
acute pain. In these cases diarrhœa was present (as in Sennft's
case), or in alternating diarrhœa and constipation, as in a case
recorded by Pye-Smith, which, however, ultimately ended in
obstruction with a favourable termination. A case recorded by
Fiedler is very remarkable, and I may quote it briefly here :—

A healthy woman, aged 34. Pains in the gastric region, wasting,
anorexia were observed, but "never jaundice or actual gall-stone colic."
Two months later increased pain in the epigastrium, then in the right
lumbar region, and lastly in the region of the sigmoid flexure. Vomiting
was frequent. The left thigh was constantly drawn up against the
abdomen. Severe pain in the right (?) iliac region. A tumour was

felt. Two months later a gall-stone was passed, consisting of three concentrically laminated portions, showing signs of mutual friction. It had the enormous weight of 46 grm. (710 gr.), and contained as much as 96 per cent. of cholesterin. From that time all discomfort and the contraction of the thigh disappeared.

6. *Diffuse Hepatitis (Cirrhosis Hepatis) due to Cholelithiasis.*

Since the publication of the works of Hanot and of Charcot and Gombault, cholelithiasis has been included among the causes of cirrhosis of the liver.

The fact that diffuse hepatitis occurs in connection with cholelithiasis was, indeed, previously known. Gubler, Virchow, Lebermeister, and others had observed such cases and had already discussed the connection of the liver disease with the cholelithiasis. Moreover, Meyer and Legg had already shown, by experiments on cats and rabbits, that ligature of the common duct caused increase of the interstitial tissue in the liver.

That diffuse hepatitis and true cirrhosis may result from cholelithiasis is, I think, beyond question, but this sequence is by no means a common one. Among twenty-three post-mortem examinations carried out in my clinics in Königsberg and in Strasburg on patients dying from cirrhosis of the liver, of which I have adequate notes, cholelithiasis was present in four; and among sixty-three sets of full notes of non-fatal cases diagnosed as examples of cirrhosis hepatis, there are twelve at most which afford adequate grounds for assuming that chole-lithiasis existed. Since Charcot wrote, the general tendency has been towards the view that biliary obstruction is the exciting cause of the connective-tissue-increase in the liver in cases of calculous cirrhosis. On the other hand, it certainly has always been admitted that the presence of gall-stones has in itself an irritative action on the walls of the biliary passages, and thus aggravates the influence of the biliary obstruction.

In the first place, the results of experiments bear witness to the importance of biliary obstruction in this connection. As Legg and Meyer had already done, Charcot and Gombault produced interstitial hepatitis by tying the common duct in animals. On the other hand, it is very questionable whether these results suffice to explain the development of calculous cirrhosis in human beings. Chambart soon afterwards found

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that it is not a true diffuse interstitial hepatitis which develops
after ligature of the common duct. The investigations of
Chambart and, after him, of Beloussow, Steinhaus, and Pick
show rather that immediately after the ligature, and probably
as the result of extravasations of bile, foci of circumscribed
cellular necrosis are produced in the peripheral portions of the
acini. These may lead to circumscribed suppurations, or to
circumscribed connective tissue increase.

As has been already stated (under *hepatitis sequestrans*) such
focal necrosis occasionally occurs in the liver in cholelithiasis;
but the observations hitherto made do not show that the con-
nective tissue growth in calculous cirrhosis originates from such
foci. No doubt cirrhosis of the liver is developed often enough
not only in cholelithiasis, but also in cases of biliary obstruc-
tion, from various other causes; but, on the other hand,
it must be noted that among the cases of cholelithiasis with
cirrhosis there are many in which there is no considerable
jaundice, as in the cases of Liebermeister, Ducastel, Metten-
heimer, Martineau (quoted by Mangelsdorff), and others. The
following facts also indicate that, in addition to biliary obstruc-
tion, another and more direct influence of the concretion upon
its surroundings comes into play. Among the fifty-two more
or less undoubted examples of cirrhosis accompanying chole-
lithiasis, collected by Mangelsdorff, there are sixteen in which
calculi were present in the intrahepatic ducts, often in large
numbers. Very probably infection of the bile is here also the
determining factor, and this is most readily engendered in the
immediate neighbourhood of the concretions.

Hanot, and, following him, Charcot and Gombault, held the
view that in cases in which jaundice is the cause of cirrhosis,
the liver is attacked by that form of hypertrophic cirrhosis which
is attended with jaundice; and, according to him, this is also
the form assumed by calculous cirrhosis.

It is not my intention to enter here into the merits of the
frequently-contested views of the above-mentioned authors.
From my own experience, and from the available examples
which the literature supplies, I do not think that hypertrophic
cirrhosis is specially frequent as a result of cholelithiasis. In
the cases of cirrhosis which I have seen in connection with
cholelithiasis, or signs of that condition, the liver has always

been moderately large, with or without well-marked jaundice. The connective tissue increase has been chiefly interlobular, but has extended more or less deeply from the interlobular spaces into the lobules. On the other hand, in no single instance of hypertrophic cirrhosis which has come to an autopsy in my clinics at Königsberg and Strasburg has cholelithiasis been present.

Calculous cirrhosis is of anatomical rather than clinical interest. Cases in which this complication is clinically conspicuous, that is to say, in which it is the factor determining the features of the disease during life, are very rare. As a rule, the still incipient process in the liver presents itself only, as Thierfelder remarked, as a secondary condition, at the autopsy. There are cases, however, in which cirrhosis of calculous origin is in itself fatal, and Litten quotes two excellent examples of this. In such cases the symptoms and course of the disease do not appear to present any exceptional features, varying as they do in cirrhosis in general ; but typical examples do occur in which ascites is far the most prominent phenomenon. Here, again, I may refer to Litten's observations.

The diagnosis of the dependence of the process upon calculi is probably in such cases of advanced cirrhosis only possible when, from the history (of gall-stone colic), or in some other way, the antecedent cholelithiasis can be established. The recognition of diffuse hepatitis due to cholelithiasis is seldom reached in the early stages, and as far as my own experience goes, I do not think that much stress should be laid, in this connection, upon the occasional enlargement of the spleen, since this symptom, which under other circumstances is of so much importance for the diagnosis of incipient cirrhosis, is too frequently met with in cases of cholelithiasis apart from any secondary hepatitis.

7. *Malignant Growths—Cancer of the Biliary Passages.*

It is necessary here to discuss cancer of the biliary passages in some detail, because cholelithiasis is almost the sole cause of that disease, and because it is not an uncommon sequel of cholelithiasis. The close connection which exists between cancer of the biliary passages and cholelithiasis has, nevertheless, only been recognised for little more than 20 years. It

is true that Klob had pointed out, as early as the year 1856, that concretions are found in the gall bladder in all cases in which it is the seat of villous carcinoma, and Frerichs had emphasised the frequency of the presence of calculi in association with carcinoma of the gall bladder.

Klebs and Willigk (1869) appear to have been the first to clearly assert that the cholelithiasis is the cause of the carcinoma. Hilton Fagge next, in 1875, first called attention, in his observations already referred to, to the important influence frequently exerted by the occurrence of such carcinomata upon the course of cholelithiasis. More recently Schüppel, Kraus, Marchand, and Zenker, among others, have discussed the question, and, as the result of their work, the dependence of carcinoma of the biliary passages upon cholelithiasis has become generally recognised. The most recent statistics of Courvoisier and Brodowski (quoted by Janowski) are very conclusive on this point. Courvoisier met with gall-stones in seventy-four out of eighty-four cases of carcinoma of the gall bladder, and Brodowski did not fail to find them in a single one out of forty cases of the same condition.

Primary carcinoma of the biliary passages assumes, as Schüppel says, both hard and soft alveolar and villous forms. It occurs most commonly in the gall bladder, and here produces infiltrations which may be as thick as a finger, and which involve a large section, or even the whole, of the bladder wall. Thus tumours are not unfrequently produced as large as a fist, enclosing the contracted cavity of the gall bladder, which is filled with broken-down purulent material and more or less numerous calculi of various sizes. The carcinomatous tumour so produced often spreads by direct extension to the neighbouring hepatic tissue, and the new growth may also spread along the wall of the cystic duct towards the hilus of the liver, and may even reach the hepatic and common ducts, either by direct extension or in the form of separate nodules. The new growth may also extend along the lumen of the duct from the gall bladder even as far as the common duct.

Metastatic growths in the liver are, according to Courvoisier's statistics, much less common. On the other hand, the gall bladder tumour may be of small size. The gall bladder may remain concealed beneath the border of the liver, although exhibiting

extensive infiltration of its wall, as in a case recorded by Lang Heinrich. On the other hand, the distended gall bladder may project as a fluctuating tumour far beyond the border of the liver, and the presenting portion of its wall may be normal, so that it presents all the characters of a simple dilatation, as was the case in two examples reported by Kraus. In both of these there was a cancerous growth at the neck of the gall bladder. In one case, in which the gall bladder was filled with apparently normal bile, the new growth had extended by continuity to the liver, where it had already formed a cancerous nodule as large as an apple. In the other case the gall bladder was distended till it was larger than a goose's egg, but no longer contained any bile, being filled, on the contrary, with a thin, brownish fluid. In this instance there were, in addition, five large metastatic nodules in the liver.

In most cases of advanced carcinoma of the gall bladder, adhesions are formed with the colon, with which fistulous communications are often developed. As the result of narrowing of the colon, obstruction may occur, as in a case of Socin's (see Courvoisier, p. 291). Much less commonly adhesion takes place between the gall bladder and the duodenum, and fistulæ are formed between them, as in a case of Paulicki's (quoted by Cohn, No. VIII.).

As already mentioned, the new growth has a special tendency to spread towards the hilus of the liver, whether from extension of the growth along the cystic duct, or by encountering metastatic growths in the lymphatic glands in the hilus. From the hilus the new growth may extend to Glisson's capsule or into the liver itself, and so compress the intrahepatic ducts. The trunk or intrahepatic branches of the portal vein may also be compressed, and within the liver the growth often penetrates into the lumen of the portal branches. Thrombosis of the trunk or larger branches of the portal vein is thus by no means a rare, and is even a comparatively frequent cause of ascites.

In the bile ducts cancer may occur at any spot, either within or without the liver. Its most common seat is at the duodenal end of the common duct, and next to this at the point where the cystic opens into the common duct, and at the bifurcation of the hepatic duct. It usually presents itself in the form of an infiltration of the wall of the duct which is narrowed or occluded.

The mucous membrane covering the infiltrated area is frequently completely or almost completely unaffected. Such changes in the bile ducts are easily overlooked or misinterpreted, as Schüppel observed. Large tumours originating from the ducts and not from the gall bladder appear to be of rare occurrence. I find a case quoted by Mangelsdorff from von Plazer in which a cancerous nodule as large as a fist is stated to have been present on the common duct, but I have unfortunately not been able to procure von Plazer's original paper.

As has been repeatedly mentioned, carcinoma of the bile passages is not unfrequently developed in the course of cholelithiasis, and the diagnosis of the condition when gall-stones are present is often a matter of difficulty. With carcinoma of the gall bladder the difficulties are not as a rule so great. Very commonly there is nothing whatever in the history pointing to cholelithiasis; dyspepsia, a rapidly increasing cachexia, or the appearance of a tumour, being the earliest signs by which the disease reveals its presence. As a rule jaundice is only developed at a later period, although it is only in the minority of cases that it is absent throughout (according to Courvoisier's statistics, only in 27 per cent.).

The tumour is situated in the region of the gall bladder, is usually nodular and hard, and is almost always tender on palpation throughout. It is not usually, as Murchison stated, but only in the minority of instances, adherent to the abdominal wall, but moves upwards and downwards with the liver with respiration. Sometimes such tumours steadily and rapidly increase in size, so that their growth can be clearly recognised from week to week.

Arterial bruits may be audible over cancerous growths in the liver, as Rovighi frequently observed. I have as yet formed no judgment based upon my own experience as to the diagnostic value of this symptom, but Gabbi has heard such bruits over the liver and in the region of the gall bladder in cases of gall-stone colic.

Not very uncommonly the presenting tumour is smooth and fluctuating, and appears to be a distended gall bladder, and sometimes, indeed, there is simply a dilatation of the gall bladder to be made out, although its wall is the seat of carcinoma. Under these circumstances the question is settled by

an exploratory puncture. If instead of bile this yields cancerous detritus, or possibly pus, hæmorrhagic fluid, or highly albuminous bile, the evidence is in each instance in favour of carcinoma. If normal bile is obtained, this is evidence against, although it does not absolutely exclude, such a diagnosis. (Conf. p. 165.)

As a rule, when carcinoma exists the exploratory puncture of the tumour yields no fluid at all, except a little blood; but now and then small particles of the tumour are obtained, the microscopical examination of which establishes the diagnosis. In not a few cases the condition of the liver is conclusive. A general enlargement is exceptional, and when jaundice is present proves nothing, since mere biliary obstruction is also capable of producing considerable enlargement. If there be a diffuse carcinoma of the organ a conspicuous hardness of its lower border can usually be made out. Nodular growths in the liver are very significant. Such metastatic tumours are sometimes hard and sometimes soft; they are seldom tender, unless suppuration is taking place within them. On the other hand, a nodular gall bladder is almost always very painful.

Enlargement of the spleen has not here the great importance for differential diagnosis which it has in hepatic carcinomata in general. Leichtenstern has given numerical proof of its rarity in carcinoma of the liver, but correct and important as this observation is, in the cases under discussion, the association of splenic enlargement with carcinoma is at any rate not very rare, since cholelithiasis itself is often attended by enlargement of the spleen. Splenic enlargement has its due importance, when the question arises of the significance of a complicating ascites, for ascites suggests new growth if duffuse hepatitis can be excluded, and the absence of splenic enlargement lends important aid in the exclusion of cirrhosis.

In a good many instances the course of the illness tends materially to facilitate the diagnosis of these cases of carcinoma of the gall bladder. When such carcinoma is present cachexia soon makes its appearance, whereas in cholelithiasis this condition is only developed after a long period, and usually after long-standing jaundice. In 6 months, at the latest, a case of carcinoma usually terminates, whereas the latter disease often lasts for years.

The recognition of carcinomata of the bile ducts is a matter

of much greater difficulty. These also have their origin almost exclusively in cholelithiasis, but only calculi in the bile ducts have a share in their causation, and consequently they are met with in the cases in which cholelithiasis itself produces symptoms. The tumours are small unless the gall bladder becomes involved in the process, and metastatic growths seldom occur, because the new growth appears to increase but slowly, and the absolute biliary obstruction which it causes proves fatal, as a rule, before metastasis takes place. In some cases the complete absence of bile from the intestine may excite suspicion, for this is unusual in calculous obstruction, whereas it is seldom wanting with carcinoma of the biliary passages.

It would be of great value for diagnosis to obtain an approximate notion of the degree of frequency with which such carcinomata of the bile ducts occur in cases of cholelithiasis, or at any rate may safely be assumed to be present during life. Adequate material for this purpose is however not yet forthcoming. The older statements are not reliable, since these small new growths have obviously often been described as simple thickenings of duct-walls, cicatricial structures, ulcerations of the mucous membranes, &c.

Among cases operated upon in recent times, almost always on the assumption that cholelithiasis existed, I have found seventy in which there was conspicuous jaundice, and in which the question of new growths in the bile ducts might have arisen. In thirty-six out of these seventy cases either an autopsy, or an operation, threw light upon the condition of the bile ducts. Of these thirty-six cases four, with carcinoma of the pancreas (apart from cholelithiasis), may be excluded, since the symptoms pointed to the diagnosis of carcinoma of the pancreas, or at any rate did not point to that of cholelithiasis. Among the remaining thirty-two cases there were eight in which there were changes in the bile ducts, which were certainly or probably carcinomatous. There was, in addition, in one case carcinoma of the papilla, and in five others carcinoma of the head of the pancreas. Cholelithiasis was only present in two of these pancreatic cases, but in my opinion the diagnosis of probable cholelithiasis was justified in the three other cases also. There were, moreover, several cases of fibrous stricture of the common duct, of which some were perhaps carcinomatous.

Hence in making a diagnosis it must be taken into account that in about half the cases of apparent cholelithiasis with chronic jaundice there exists in addition to, or in place of that condition, carcinoma of the biliary passages.

ADDENDUM.

1. *Cholelithiasis and diabetes.*—Cases have been placed on record by Ord, Kraus, Loeb, and Hull in which diabetes mellitus has been observed in association with gall-stone colic. Sweet* observed it to follow obstructive jaundice, and Gans " has constantly observed the excretion of sugar during and immediately after the attack in a series of cases of gall-stone colic." Kraus, too, makes a similar statement. The authors mentioned are inclined to bring the two diseases into a causal relationship, Ord, Loeb, and Gans holding that the gall-stone colic is the cause of the diabetes.

I cannot as yet give my adhesion to this view. In no one of the cases was it proved that diabetes was not previously present, and apart from such proof it is certainly not permissible to conclude that there is a causal relationship, seeing that both diseases, cholelithiasis and diabetes, are quite common, and no special explanation is required of their occasionally attacking the same individual. That the diabetes undergoes a sudden aggravation after the colic attacks proves nothing, since this result follows a very great variety of lesions which affect diabetic patients. At any rate I cannot confirm from my own experience the frequent appearance of sugar in urine in connection with gall-stone colic. I have never met with it.

2. Pernicious anæmia has also been observed to develop after cholelithiasis, and Georgi has described such a case in detail. There is no reason to doubt the possibility of cholelithiasis leading to pernicious anæmia, seeing that it can produce in various ways injurious effects upon nutrition and the constitution of the blood. Jaundice of any kind, including that due to cholelithiasis, is capable of causing severe anæmia, and under certain conditions the anæmia may assume a progressive and pernicious type.

* I have unfortunately been unable to consult Sweet's work in the original.

Nevertheless, the cases in which progressive pernicious anæmia has actually occurred, as a sequel of cholelithiasis, are very few, and there is no sufficient reason for assuming the existence of any intimate relationship between these two diseases.

CHAPTER VIII.

TREATMENT OF CHOLELITHIASIS.

1. *Experimental Data.*

The stagnation of bile in the biliary passages tends in itself to favour the formation of concretions, but it also favours the infection of the bile. This is probably not without influence even upon the initial formation of stone-producing precipitates, and is undoubtedly of the very greatest importance for the further development of cholelithiasis. Hence it is under all circumstances one of the aims of the treatment of cholelithiasis to take care that such stagnation is avoided. One may further suppose that concretions already formed will be much more readily borne away by an active stream of bile. However, this is probably only true of concretions which are still soft and float in the bile, whereas upon harder formations, which are heavier than the bile, the bile stream, which always flows very slowly, has probably hardly any influence as a moving force. Such calculi, when they cause obstruction, will be to some extent forced onwards by the pressure of the retained bile, acting in one direction only, but their progress is chiefly due to the muscular contraction of the walls of the bile ducts.

The outflow of bile is caused—

(*a*) By contraction of the gall bladder, which appears to be excited by the entrance of chyme into the duodenum.

(*b*) By the pressure of the diaphragm upon the liver in inspiration, and by the action of the abdominal pressure which accompanies many active muscular acts.

(*c*) Much less simple is the operation of the third factor which determines the flow, that is to say, secretion.

Both the amount and the consistence of the bile secreted are of importance, for the bile will flow more abundantly the larger the quantity that is secreted, and the less the resistance which it meets with in the biliary passages. This resistance is much greater when the bile is viscid than when it is more fluid.

The viscosity or greater fluidity of the bile chiefly depends upon the amount of mucus contained in it, and this depends not upon the condition of the biliary secretion, but upon the condition of the mucous membrane of the passages.   Yet experience shows that, speaking generally, bile which contains more water is more fluid than that which is more highly concentrated, and the bile is, as a rule, thinner and more fluid, the more active the secretory process.

It seems then that to endeavour, when treating cholelithiasis, to increase the bile flow, by stimulating secretion, is correct in principle.   From time to time many drugs have been recommended for this purpose, but as yet authors have not been able to arrive at any agreement as to their value.

Numerous experiments upon animals have been carried out by Bidder and Schmidt, Kölliker and Müller, Mosler, Ritter, Spiro, Röhrig, Schiff, Sokolow, Klikowitsch, Lewaschew, Rutherford and Vignal, Prévost and Binet, Röhmann, Gorodecki, Nissen, and others, bearing exclusively or in part with this point, but their results are in many instances contradictory. These divergencies, the causes of which have been recently explained by Stadelmann, render a definite conclusion difficult. However, the following seem to me to be the conclusions to be drawn from these experiments. Many substances when taken into the stomach, and more surely still when introduced into the duodenum (Rutherford), appear to produce, under certain conditions, a slight increase of the biliary secretion.   However, the influence of these substances upon the secretion of bile is uncertain, and never a potent one. Sometimes they fail entirely to produce increased secretion, and the increase is always slight and is very transitory.   In general, the increase is only an atall constant in curarised animals, whilst in animals breathing spontaneously their effects are easily obscured by the fluctuations of the biliary secretion, dependent no doubt upon respiration, &c.   Among these drugs are rhubarb, aloes, senna, euonymus, podophyllin, the preparations of mercury, turpentine, ether, &c.   These are for the most part drugs which excite peristalsis of the intestines, and which, in large doses, have a purgative action.

It appears that their effect upon the secretion of bile is connected with this action of theirs upon the intestine, and in association with active spontaneous peristalsis of the

bowel, remarkably active biliary secretion has been observed (Röhrig). But frequently the opposite effect has been observed, and when more active aperients have been employed, which cause much irritation of the intestinal mucous membrane, *e.g.*, croton oil (Rutherford and others) the secretion of bile has been seen to be diminished. Rutherford even lays it down as a rule that the cholagogue effect of the drugs referred to is no longer perceptible when their purgative action comes into play.

Castor oil and olive oil appear, like fats in general, to have hardly any effect upon the secretion of bile, and in opposition to the recent experiments of Rosenberg, which point to such an influence, are to the negative statements of numerous other authors. No cholagogue action can be assigned to the alkaline carbonates and the purgative alkaline salts ; indeed they often diminish the biliary secretion.

Neither is water a cholagogue. In numerous experiments water has been introduced into the stomach or intestines of animals in quantities varying from 100 cc. to whole litres, and these experiments (among which those of Loewenton, Müller, and Nissen must be specially mentioned) have shown that at most a quite insignificant increase of the biliary secretion is produced even by the administration of very large quantities of water, either cold or warm, whether it be pure water or Carlsbad water (Thomas), and that even such slight increase is sometimes wanting. On the other hand, a very conspicuous increase of the secretion of bile can be brought about by means of salicylates (Rutherford and Vignal, Lewaschew, Prévost and Binet, and others) the salts of the bile acids (Schiff, Sokolow, Prévost and Binet, and others), and also by poisoning with arseniuretted hydrogen, or toluene-diamine (Stadelmann, Affanassiew, and others), that is to say, speaking generally, by all substances which have the peculiar effect upon the red blood corpuscles of causing the expulsion of hæmoglobin from them.

To this group of substances belong also the salts of the bile acids, and according to Nissen (and Chivone, quoted by Nissen), sodium salicylate also. Moreover, it is certain only as regards these two substances that they exhibit their cholagogue action even in small, non-poisonous doses, and this it is that determines their cholagogue action ; for although in the forms of poisoning

referred to there is unquestionably an increased formation of
bile, stagnation easily results on account of the viscidity of the
bile that is formed.   On the other hand, digestion exercises the
most potent influence of all upon biliary secretion. After a meal
there occurs a conspicuous and lasting increase of the secretion
of bile, which reaches its maximum in from 3 to 16 hours ; and
resorption of chyme appears to be exciting cause of this increase
of the activity of the liver (Röhrig).   Among individual food-
stuffs, albuminous substances are the best cholagogues, whereas
the action of carbohydrates and fats is slight (Ritter and others) ;
but a mixed meal produces the best effect, on account of the
active chymification to which it leads.

All these true cholagagues, viz., a meal, the alkaline bile salts,
and salicylates in non-poisonous doses, cause increased secretion
of bile, which is considerably more fluid than usual.   In this
respect the increased bile stream which they produce is to
be distinguished from accidental variations in quantity.   In such
fluctuations the concentration of the bile remains unaltered, or
the secretion, although more abundant, only shows a slight
diminution of concentration.

There is little that can be said as to the possibility of in-
fluencing the composition of the bile apart from the amount
of water contained in it, i.e., its concentration, in any way which
is of therapeutic value.

The reaction of the bile should be neutral or alkaline, but
hardly anything is known concerning the variations in its
reaction under physiological conditions.   Administration of
alkalies (as by the introduction of sodium carbonate into the
stomach, in large quantities) does not alter it ; that is to say,
does not increase the alkalinity of the bile.

In the same way hardly anything is known as to the depen-
dence of the relative amounts of the individual normal con-
stituents of the bile upon the nature of the diet, save that it
appears that on a nitrogenous diet the bile is richer in salts of
the bile acids.   When administered by the mouth the following
drugs pass into the bile, viz., potassium iodide (Mosler),
potassium chlorate (Prévost and Binet), mercury, copper, lead,
and other metals, salicylic acid, turpentine, terpinol, terpin
(Prévost and Binet), and among pigments, indigo-carmine,
sodium indigo-sulphate, aniline red (Chronsczewski), cochineal,

and fuchsin. Alcohol does not so reappear, neither do quinine (Mosler), atropine, muscarine, strychnine, kairin, nor antipyrin (Prévost and Binet); chloral also appears not to enter the bile at all, or only in very minute quantity.

Among the substances which reappear in the bile are many which, on account of their antiseptic properties, are capable of exerting a beneficial action. For instance, it is only necessary to recall the favourable action of potassium chlorate upon infective catarrh of the urinary passages. It is to be regretted, therefore, that investigations bearing upon the quantities in which these substances pass into the bile have not as yet been carried out. From the experiments which Dr. Weintraud has made with potassium iodide, and the statements of Prévost and Binet with regard to turpentine and the like, it appears that these substances only enter the bile in very scanty amounts.

2. *General Treatment of Cholelithiasis.*

(a) *Diet, clothing, exercises, and the like.*—Although so little is definitely known of the effect of diet in cholelithiasis, it is obvious that harmful foods and excesses should be avoided which are calculated to have an injurious action upon the liver, or to produce digestive disturbances; such as overeating, abuse of alcoholic drinks, excessive taking of spices, &c. When, as is frequently the case in cholelithiasis, dyspepsia and irritability of the digestive organs already exist, these call for due attention. Cholelithiasis does not call for any further restriction of the dietary, and on this point the experience of medical men is in complete accord with the teaching of experiment. Meat and other albuminous articles of food favour the secretion of bile, and it is only on account of complications that they may have to be prohibited. The meals should not be taken at too long intervals, in order that the stagnation of the bile in the gall bladder may be, as far as possible, prevented. Breakfast, coming as it does after the long night's fast, should not be taken too sparingly.

As to clothing, it should be seen that abdominal breathing (the inspiratory contraction of the diaphragm) is not interfered with; and tight strings in corsets, belts, or straps are therefore harmful. Walks are very necessary, and mountain climbing is

excellent, since it calls forth energetic respiratory movements.
Moreover, gymnastic exercises and abdominal massage are
strongly to be recommended if active bodily exercise cannot
be obtained.

All such proceedings appear to have their best effects in the
early morning.   They do not all indeed have a direct influence
upon the evacuation of the bile, but owe their favourable action
chiefly to the fact that they favour peristaltic action and the
abdominal circulation.   In this way also are to be explained
the beneficial effects not unfrequently induced by cold river and
sea bathing, and hydropathic treatment. .

Certain conditions arising in the course of cholelithiasis, to
which reference will be made later, may call for the employment
of cholagogues.   In the general treatment these can have no
place, since no drug has a cholagogue action comparable to that
of a full meal.   Here again there is no conflict between medical
experience and the results of experimental investigation.
Neither has such experience made us acquainted with any drug
which has any definite effect, or even which has obtained any
measure of general favour amongst physicians.

(b) On the other hand, medical experience appears to speak,
almost with one voice, for the beneficial action of warm sodium
waters, and warm sodium waters containing Glauber's salts, in
cholelithiasis.   Among the former that of Vichy, and among the
latter that of Carlsbad, enjoy the greatest popularity ; and on the
ground of the constitution of their waters Ems and Neuenahr
must be mentioned with Vichy, and with Carlsbad, Bertrich
(district of Coblenz) and Stubnya and Ofen in Hungary.
Carlsbad possesses the hottest springs (70° C., 158° F.), which
are further distinguished by the very considerable amount of
carbonic acid which is nevertheless present.   Of the sodium
waters containing Glauber's salts Ofen alone, with springs up
to 62° (144° F.), approaches it.   The Bertrich water closely
resembles that of Carlsbad, and is also rich in carbonic acid, but
its temperature is only 32° C. (89° F.).   Of the above-mentioned
sodium waters, that of Vichy is by far the richest in sodium
carbonate.   The temperature of the springs of Vichy reaches
44° C. (111° F.), those of Ems 46° C. (115° F.), and those of
Neuenahr 35° C. (95° F.).   The amount of carbonic acid is con-
siderable at all three places, and not conspicuously different.

I regard it as an established fact that the Carlsbad treatment exercises a most beneficial effect upon the course of cholelithiasis. In not a few cases I have seen long-lasting and dangerous incarceration of gall-stones reach a favourable termination at that place. The patients passed gall-stones during attacks of comparatively slight severity, and I have seen the cases, afterwards and for years together, run so favourable a course that a cure appeared to have been attained.

The action of this course is a complex one. The importance of the manner of living associated with the course must not be under-estimated, but a special influence of the mineral water itself certainly cannot be denied. That this is due to its cholagogue action appears, after what has been said, very unlikely; but, on the other hand, the bowel is better emptied than usual, and peristalsis is excited, whilst the mucous membrane is slightly stimulated by the hot water containing Glauber's salt, and by the carbonic acid which it gives off. By all these means the circulation in the abdominal organs, including the liver, is probably stimulated and the hot saline water probably has a similar action.

Just as the mucous membrane of the stomach and intestine affected by catarrh thus experiences a favourable "alterative" effect, so a similar effect may be produced upon the mucous membrane of the biliary passages. Prout, who was the first to advise the drinking in large draughts of hot water, containing 10—15 per cent. of sodium carbonate, in gall-stone colic, held that the hot water acted as a poultice to the diseased part. According to my own experience, the saline water taken hot has a very favourable action even at home ; and even pure hot water, taken in large quantities, is of good service in the treatment of cholelithiasis.

Krull and Mosler recommended the injection of large quantities of warm water into the large intestine, and I believe that I can confirm its good effects in the treatment of cholelithiasis. It is probable that in many respects the warm water has a similar effect whether introduced into the large intestine or into the stomach ; and moreover it is possible that, as Krull himself believed, the distension of the colon by the injected water may exert a gentle tension upon the biliary passages, and so excite contractions in them.

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3. *Special Treatment of Cholelithiasis.*

(*a*) The treatment of gall-stone attacks is chiefly directed against the pain. With this object, as soon as the diagnosis is established, morphia should be given subcutaneously and not in too small doses (1—2 cgm., $\frac{1}{6}$—$\frac{1}{3}$ gr. as a dose). As a rule, larger doses at longer intervals are much more serviceable than smaller ones frequently repeated.

Large poultices applied to the right hypochondrium are also very effectual, as also are prolonged baths from 35°—38° C. (95°—100° F.), and the drinking of hot water in repeated doses of about 100 cc. (3½ ozs.). At first, when vomiting is present, it will be constantly vomited again, as Murchison stated, but after a short time the vomiting, and the pain too, will usually be relieved.

Murchison recommends atropine instead of, or in addition to, morphia. According to my experience it may be safely given subcutaneously, in conjunction with morphia, in doses up to 1 mgm. ($\frac{1}{60}$ gr.), 1—2 cgm. ($\frac{1}{6}$—$\frac{1}{3}$ gr.) of morphia being given at the same time.

Chloroform also is often employed with most excellent effect. It may be most safely inhaled, only to quite superficial narcosis, of course, for anæsthesia has after effects. It has also been given internally (in the form of one or two capsules, each containing a gramme (15 grs.)) with good results.

Chloral has also been given in place of chloroform in frequent small doses (*e.g.*, in doses of ·5 gramme up to the amount of 2 grammes (8—30 grs.) in 2 hours). I have frequently tried it, but have not observed any particular effect, and it is certainly erroneous to suppose that it is to any appreciable extent converted into chloroform in the blood, and as such exercises an influence upon the bile ducts.

According to Kraus, antipyrin has a good effect when given quite at the commencement of the attack; but later, when the attack has already lasted for hours, it is not without danger, owing to the possibility of collapse.

The same is true of sodium salicylate, which I have repeatedly given, with apparently favourable result, in a single dose of 2—3 grammes (30—45 grs.) at the beginning of the attack. Kraus has correctly maintained that the sweating produced

by the drug gives relief to the patients, yet in my experience pilocarpine has no good effect. Lastly, we have the recommendation of Quisling, who observed great relief follow the application of an elastic bandage to the abdomen in seven cases of gall-stone colic.

The above recommended lines of treatment, which chiefly serve for the relief of the pain, also best satisfy, according to my experience, the other main indication, viz., the furthering of the expulsion of the calculus, seeing that the worst pain of all, the intolerable colic, is due to the muscular spasm in the bile ducts in which the stone is embraced. The narcotics which arrest such spasm at the same time lend effectual aid to its passage. In illustration of this effect, one may point to the example of intestinal obstruction, in the treatment of which the narcotics are unquestionably the most efficient drugs.

On the other hand, he who prefers to employ cholagogues will unquestionably do best in giving the salts of the bile acids, at any rate when, as is so often the case, jaundice is absent or is at least of very slight degree. The cholagogue action of these salts appears at any rate to be unquestionable, and they are innocuous when administered by the stomach. In rare cases I have tried these, like all other cholagogues, without any good result, and I must say the same of Durand's treatment also. I have been specially dissatisfied with large doses of olive oil, which reduce the patients by destroying their appetites.

An obvious result, i.e., the passage of calculi after longer or shorter attacks, is occasionally seen after all such treatments, including Durand's, and after olive oil. However, this is a rare occurrence, and certainly in no way dependent upon the treatment employed. None of these treatments has obtained general acceptance.

I have never seen any good result from bleeding. Venesection, which was formerly resorted to in colic, would no longer be recommended by any one; and, in my opinion, local bloodletting should be entirely dispensed with. An emphatic warning must be given against its employment, as by the application of leeches, seeing that in jaundice a hæmorrhagic diathesis often exists, and bleeding may therefore prove dangerous.

The fever of cholelithiasis cannot be lastingly influenced by antipyretics. Quinine given in large doses during the apyretic interval now and then averts the intermittent febrile attacks, but never more than temporarily; and, for my part, I have seldom obtained this result. When the febrile attack has once commenced, the temperature may be brought down and the febrile disturbance removed by antipyrin or phenacetin in one or more doses up to 1 gramme (15 grs.); but I am under the impression that, in biliary fever especially, the effect of these antipyretics is very temporary, and that in such cases these drugs, if given repeatedly, lose their effect more rapidly than in other cases. Moreover, in many cases in which collapse exists, or threatens, the warning of Kraus against the employment of antipyretics is thoroughly justified. Collapse when it threatens must obviously receive its appropriate treatment.

Among further secondary conditions cholecystitis as a complication, and acute perforation-peritonitis following rupture of the biliary passages, may call for prompt measures, which will be discussed under the head of the surgical treatment of cholelithiasis. When the attacks are protracted, one must be less liberal in the employment of narcotics. In such cases I have always obtained the best results from the early commencement of a course of hot Carlsbad water, and copious injections into the bowel. These measures bring about the unloading of the bowels in the most desirable manner, and I concur fully in the warnings given by other authors against the employment of active purgatives.

(b) The statements made in the second section of this chapter hold good for the treatment of irregular cholelithiasis. I must here once more express the conviction, based upon experience, that by the mineral-water treatments already mentioned by injections as recommended by Krule, and by massage, the best, and sometimes surprisingly good results, are obtained. A gloomy prognosis is, at any rate, not justified until such means have been seriously tried, and, until the patient has gone through a course at Carlsbad, the uselessness of internal treatment should not, in my opinion, be assumed.

Of the various forms which irregular cholelithiasis assumes, intestinal obstruction from gall-stones alone calls for mention here. In this, as in other forms of obstruction, treatment by

opium is specially to be recommended, seeing that, in obstruction from gall-stones, spasm of the muscular coat of the intestine undoubtedly plays an important part. The calculi which produce obstruction are often not large enough to fill the lumen of the relaxed bowel, and hence we may conclude that spasmodic contraction of the intestinal wall occurs around the stone, and that this is the cause of the occlusion of the bowel. Such contractions will occur the more certainly if, as is so often the case, the intestinal mucous membrane be ulcerated at the part in which the calculus lies. We learn from what is seen in the urethra, the œsophagus, and the rectum how easily contraction of the muscular coat originates from such ulceration of mucous membranes. Ulceration of the mucous membrane in obstruction due to gall-stones very frequently leads to perforation of the intestinal wall ; and, in view of the possibility of such an event, treatment by opiates is also indicated.

4. *Surgical Treatment.*

1. Even in the course of an attack of gall-stone colic operative interference may become necessary. Rupture of the gall bladder or duct may result and lead to general peritonitis, and when such perforation-peritonitis can be diagnosed with sufficient certainty, laparotomy is, in my opinion, called for, and may lead to recovery (Case VI.).

Up to the present time no unanimity of opinion has been reached on the question whether the operation should be performed as soon as possible after the occurrence of rupture, or whether one should wait until the primary shock has passed off. I am inclined, from what I have seen, to decide in favour of the latter course.

Acute infective cholecystitis, which, as was shown in Section VII., B. (*b*), so frequently accompanies gall-stone attacks, may also call for operation, since such bacillary cholecystitis may prove fatal by general infection or peritonitis. Case XVIII. is a striking example of the first mode of termination. I should even at that time have had an operation performed if the patient had not been in an extremely feeble condition ; at the present time I should probably do so even in spite of that.

The moment at which general infection threatens is often not easy to hit upon in individual cases.

A fatal result may follow from peritonitis, apart from any perforation, by extension of the infective process through the wall of the gall bladder to the serous membrane, as in a case recorded by Potain. In Case XIV. there was threatening of such an event, and I had therefore decided that an operation was necessary, when suddenly improvement set in.

In such cases of acute cholecystitis the operation is comparatively easy to carry out, and free from danger, since the gall bladder, which is tensely filled, always lies against the abdominal wall. Probably there exists a still wider field for operative interference in these cases, for the question may be raised whether such cases, when the presence of infective cholecystitis is definitely determined, should not always be immediately operated upon, instead of waiting until they become chronic. When they have reached this stage, the operation will very probably become necessary later on, when the conditions may be less favourable for its success. At present I do not think that an affirmative answer can be given to this question.

2. In chronic empyema of the gall bladder, when spontaneous devolution can no longer be looked for, I regard an operation as certainly called for, provided that there is no jaundice, on account of the danger of general infection, perforation, or fistula formation. In cases with clearly palpable gall bladder and no jaundice which come to operation the prognosis is favourable.

I have collected from Courvoisier's tables the operation cases which fulfil these two conditions; I have only been able to make use of eighty-nine cases, because in many instances the statements of the authors are inadequate. Among these eighty-nine cases, six proved fatal, i.e., there was a mortality of 6·7 per cent. The mortality in such cases will doubtless be still smaller when more light shall have been thrown upon the hitherto very conflicting opinions among surgeons as to the method of operating to be employed.

3. Even now the mortality among cases operated upon on account of the presence of a tumour of the gall bladder, apart from jaundice, is sufficiently small to allow of the recommendation of surgical interference, even for simple distension of the gall bladder, especially if severe disturbances due to cholelithiasis be present.

Already, in a large number of cases, gall-bladder surgery

has produced improvement and even apparent cure by the removal of gall-stones from the gall bladder. As to the prospects of operation when it is undertaken on account of the troubles which cholelithiasis causes, although it be not called for by the presence of a tumour of the gall bladder, it is as yet too soon to form a judgment. The number of such cases is as yet too small for this purpose, but the mortality does not appear to be very much greater in such cases than in those in which an operation is performed on account of an uncomplicated swelling of the gall bladder (viz., 6·7 per cent.).

4. Jaundice is of more importance for the prospects of operation. Stanmore Bishop certainly goes too far in holding, with Greig-Smith, that when jaundice is present operation is contra-indicated, but without question its presence is unfavourable. I have grouped the cases from Courvoisier's tables which came to operation, according as whether pronounced jaundice was present at the time of the operation or no. Among 173 cases without jaundice eighteen proved fatal (9·6 per cent.), and among seventy cases with jaundice thirty-four (48·7 per cent).

The prognosis is in the first place rendered worse *ipso facto* by the presence of jaundice, since patients with severe jaundice are anæmic and have less resisting power ; and, moreover, there often coexists with severe jaundice a disposition to hæmorrhages. Courvoisier has given numerical proof of the frequency of this tendency, and has insisted upon the undesirability of operation when such a hæmorrhagic diathesis exists. Moreover, and this is perhaps still more decisive, complications such as carcinoma of the biliary passages or pancreas, severe pericholàngitis or pericholecystitis, are much more commonly present in jaundiced cases ; and these not only render the success of the operation illusory, but also frequently increase the actual dangers of the proceeding.

In recommending an operation in cholelithiasis with jaundice the greatest caution should be observed. It is not sufficient to ascertain that all other means, and especially the Carlsbad course, have been tried, but the wish of the patient must be justified by the presence of serious dangers or intolerable discomfort before an operation can be considered to be called for. On the other hand, jaundice should certainly not be regarded as absolutely contra-indicating an operation. Some cases with

chronic jaundice and its attendant discomforts, which apart
from operative interference appear quite hopeless, are saved
by operation; and in my opinion this suffices to impose upon
the medical attendant the duty of considering whether an
operation is called for in cases in which this appears to be the
condition.

5. I cannot refrain from making the following remarks upon
the choice of modes of operating.   According to the results of
the operations hitherto performed, bilateral cholecystostomy is
the safest method.   For this reason I would recommend it,
except when in individual cases some special indication for
another method exists.   The objections which I find generally
raised to it do not convince me, and I hold that the fear that a
biliary fistula may possibly remain is not decisive against it,
since experience shows that a troublesome or dangerous fistula
seldom persists, provided that the common duct be free, whereas
in other cases it is almost necessary.

I think also that the fear of a fresh formation of calculi in the
gall bladder affords no adequate ground for preferring chole-
cystectomy, since calculi may form and grow in the bile ducts
also.   Again, the reasons which have been advanced for carry-
ing out the cholecystostomy in one sitting fail to convince me.

The physician who recommends a patient to submit to an
operation determines upon this course, after taking into
account, before all, the chances of a fatal result.   He
expects the operating surgeon to choose the least dangerous
method, unless there are very strong reasons to the contrary.
The fulfilment of this condition on the part of the surgeon
will greatly assist their mutual co-operation.

6. Occasionally a preliminary laparotomy is necessary for the
establishment of the diagnosis.   Under these circumstances also
the dangers introduced by jaundice are to be considered, but
for the rest the surgeon alone bears the responsibility for the
result.   The reasons for this I need not enter into.

7. In the German edition of this work I was only able to
refer to thirteen cases of laparotomy for intestinal obstruction
by gall-stones, of which only two ended in the survival of the
patients.   In one case (Clutton's) in which it was not found
necessary to open the intestine because the stone lay not far
above the ileo-cæcal valve, and could be pushed on past the

valve, its further passage was attended by no difficulty. Since then ten more cases have been published, with five recoveries (see Roguer-Gusenthal, Wiener med. Presse, 1894, one case with recovery ; Pouzet Archives Provinc. de Chirurgie, 1892, Part 1, one case of recovery; Körte, Deutsche med. Wochenschrift, 1894, four cases with three recoveries; Leudner, a fatal case ; Israel, Berliner klin. Wochenschrift, 1892, a fatal case ; Czerny and Rindfleisch in Billroth's Festschrift, a fatal case ; Tunnicliffe St. Barthol. Hosp. Report, 1892, a fatal case). Of the twenty-three cases which I know of as many as sixteen were fatal. I am, therefore, still of opinion that in intestinal obstruction from gall-stones laparotomy is not to be recommended generally.

Although the results of the ten latest cases of operation were far more favourable, the following considerations nevertheless hold good. Intestinal obstruction from gall-stones runs a favourable course without operation in 50 per cent. of the cases, and a favourable result has often followed after the impaction has persisted for a week or longer, so that an operation should not at any rate be performed early. If, on the other hand, the impaction has existed for a longer time, it is highly probable that necrosis of the intestinal wall and circumscribed peritonitis from perforation will have resulted.

This may occur in several different parts of the intestine, some of which may be far removed from the place in which the gall-stone is ultimately found, and thus may easily be overlooked at a laparotomy directed to its removal.*

* Disintegration of the stone in the intestine is seldom likely to be accomplished without injury to the intestinal wall, since these large calculi are as a rule very hard.

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INDEX.

REPORT

THIRTY-EIGHTH ANNUAL MEETING

OF THE

NEW SYDENHAM SOCIETY

HELD IN CARLISLE,

July 31st, 1896.

WITH

BALANCE SHEET FOR 1895, LIST OF OFFICERS FOR 1896-97,
AND LIST OF PUBLISHED WORKS.

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Those marked with an asterisk were not in office last year.

REPORT

The works which have formed the series for the past year are the following:—

> The Second and concluding Volume of Sir William Gull's Works. With Portrait and Memoir.
>
> A Fasciculus of the Atlas of Pathology, concluding Diseases of the Testis.
>
> The First Volume of Binz's Lectures on Pharmacology.
>
> A Fasciculus of the Lexicon of Medical Terms.

Of these the latter three have for some months been in the hands of the Society's members. The concluding volume of Sir William Gull's Works is still due. The delay has been caused by unforeseen difficulties in completion of the Biography. The whole of the book is in type.

For the current year one book has been issued, and the following may be expected to form the series:—

> I. Prize Essays on Leprosy. (Newman, Ehlers, Impey.)
> [*Already out.*
>
> II. The second and concluding volume of Binz on Pharmacology.
>
> III. A volume on Vaccination, to contain the Majority Report of the Royal Commission, and selections from the evidence brought before it, with more especial reference to possible ill consequences from its practice. With illustrations.

IV. A volume of Selected Essays, to contain, with others,
Essays on Syringomyelia, on Yaws, on Syphilitic
Affections of the Spinal Cord, on Pemphigus
Vegetans. With illustrations.

V. A Fasciculus (XXIII.) of the Lexicon of Medical
Terms.

It is possible that Naunyn's treatise on Cholelithiasis, the
printing of which is well advanced, may be substituted for
one of these.

Amongst the works which the Council has in preparation
are the following :—

Selected Papers on Actino-Mycosis. Edited by Dr. Sims
Woodhead.

A Volume of Selected Monographs on Gynecological
Subjects.

Selected Lectures from Jaccoud's Clinical Medicine.

Selections from the Works of Professor Fournier.

A Volume of Selected Monographs on Diseases of the Ear.

A Series of Volumes of Selected Clinical Lectures on Medi-
cine and Surgery from various (Foreign) sources.

Prize Essays on subjects connected with Leprosy.

The most important work which the Council has under-
taken during the past year is the one on Vaccination. The Royal
Commission on this subject has now extended its enquiries
over nearly seven years, and has issued from time to time
voluminous reports of evidence. The Commission's final
Report is expected to be ready very shortly, and will no doubt
constitute an important summary of facts, not only as to the
history of Vaccination and its efficiency as preventive of small-
pox, but of the ill-consequences which are sometimes encountered
in its practice. As these large blue books are not likely to come
into the hands of more than very few members of the profes-
sion, and are besides so detailed that they are very difficult

to consult, it has appeared to the Council that it would be of service to the profession to prepare a readable summary of their contents. The final Majority Report and recommendations of the Commission will be reproduced without curtailment, but the evidence taken and documents which constitute the appendices will be re-classified and much condensed. It is hoped that the volume will present a complete statement of present knowledge on this important subject. The Council will have the assistance of Dr. Barlow, Dr. Theodore Acland, and Dr. Knowsley Sibley in the preparation of the work.

The Treasurer's accounts were audited as usual at the end of the Society's financial year. On the 31st of December last there was a balance of £42 15s. 3d. in hand.

Ðr.   THE NEW SYDENHAM SOCIETY.—BALANCE SHEET FOR 1895.   **Cr.**

Receipts.

	£	s.	d.
Balance in hand brought forward from last account	62	2	8
Subscriptions..56 for 1859 to 1889..	58	16	0
6 ,, 1890	6	6	0
7 1891	7	7	0
92 1892	96	12	0
120 1893	126	0	0
554 ,, 1894	581	14	0
1002 ,, 1895	1052	2	0
21 1896	22	1	0
Say 1858 Subscriptions	1950	18	0
Back Volumes	117	12	9
Repayment of postage, &c., charged in Agent's Disbursement Account	43	13	6
	2112	4	3
Less deductions by Local Secretaries	30	17	5
	2081	6	10
	£2143	9	6
To Balance brought down	42	15	3

W. SEDGWICK SAUNDERS, *Treasurer.*

Expenditure.

		£	s.	d.	£	s.	d.
Artists, Editors and Translators, Printers, Paper, and Bookbinders					1548	12	3
One year's rent for warehousing stock					80	0	0
Expenses of Management:—							
Agent's Salary and Commission		232	14	10			
Disbursements (chiefly carriage of books)		110	17	8			
Advertisements		103	6	6			
Fire Insurance of Stock		15	7	6			
Treasurer's Expenses (one year)		2	15	0			
Assistant Secretary (including £3 9s. 6d. paid for stamps)		57	0	6			
					522	2	0
					2100	14	3
Balance in hand, 31st Dec., 1895					42	15	3
					£2143	9	6

Examined, compared with the vouchers, and found correct, the balance on 31st Dec., 1895, being £42 15s. 3d., at an Audit held this 2nd day of July, 1896.

<div style="text-align:right">EDWARD CLAPTON
A. E. SANSOM   } *Auditors.*
WAREN TAY</div>

London, July, 1896.

CLASSIFIED LIST

SOCIETY'S PUBLICATIONS.

Medicine.

LECTURES ON PHARMACOLOGY. By Dr. C. BINZ. Translated from the second German edition by ARTHUR C. LATHAM, M.A., M.B., Oxon. Vol. I.

"Will be welcomed by English readers. . . . . . . Cannot fail to prove useful both to students and to those engaged in actual practice."—*Lancet*, March 28, 1896.

"We are very glad indeed that the New Sydenham Society has published Dr. Binz's well-known 'Lectures on Pharmacology,' and we may at once say we have rarely read a more interesting book."—*Practitioner*, Aug. 1896.

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LIST OF PUBLISHED WORKS

Arranged according to the Year of Issue.

Vol.   1859.   (*First Year.*)

1. DIDAY on Infantile Syphilis.
2. GOOCH on Diseases of Women.
3. MEMOIRS on Diphtheria.
4. VAN DER KOLK on the Spinal Cord, &c.
5. MONOGRAPHS (Kussmaul and Tenner, Graefe, Wagner, &c.)

1860.   (*Second Year.*)

6. Dr. BRIGHT on Abdominal Tumours.
7. FRERICHS on Diseases of the Liver.   Vol. I.
8. A YEARBOOK for 1859.
9. ATLAS of Portraits of Skin Diseases.   (1st Fasciculus.)

1861.   (*Third Year.*)

10. A YEARBOOK for 1860.
11. MONOGRAPHS (Czermak, Dusch, Radicke, &c.)
12.*CASPER's Forensic Medicine.   Vol. I.
14.*ATLAS of Portraits of Skin Diseases.   (2nd Fasciculus.)

1862.   (*Fourth Year.*)

13. FRERICHS on Diseases of the Liver.   Vol. II.
15. A YEARBOOK for 1861.
16. CASPER's Forensic Medicine.   Vol. II.
17. ATLAS of Portraits of Skin Diseases.   (3rd Fasciculus.)

1863.   (*Fifth Year.*)

18. KRAMER on Diseases of the Ear.
19. A YEARBOOK for 1862.
20. NEUBAUER and VOGEL on the Urine.

Vol.   1864.   (*Sixth Year.*)

21. CASPER's Forensic Medicine. Vol. III.
22.*DONDERS on Accommodation and Refraction of the Eye.
23. A YEARBOOK for 1863.
24. ATLAS of Portraits of Skin Diseases. (4th Fasciculus.)

1865.   (*Seventh Year.*)

25. A YEARBOOK for 1864.
26. CASPER's Forensic Medicine. Vol. IV.
27.*ATLAS of Portraits of Skin Diseases. (5th Fasciculus.)

1866.   (*Eighth Year.*)

28. BERNUTZ and GOUPIL on the Diseases of Women. Vol. I.
29. ATLAS of Portraits of Skin Diseases. (6th Fasciculus.)
30. HEBRA on Diseases of the Skin. Vol. I.
31. BERNUTZ and GOUPIL on Diseases of Women. Vol. II.

1867.   (*Ninth Year.*)

32. BIENNIAL Retrospect of Medicine and Surgery.
33. GRIESINGER on Mental Pathology and Therapeutics.
34.*ATLAS of Portraits of Skin Diseases. (7th Fasciculus.)
35. TROUSSEAU's Clinical Medicine. Vol. I.

1868.   (*Tenth Year.*)

36. THE Collected Works of Dr. Addison.
37. HEBRA on Skin Diseases. Vol. II.
38. LANCEREAUX's Treatise on Syphilis. Vol. I.
39. ATLAS of Portraits of Skin Diseases. (8th Fasciculus.)
40. CATALOGUE of Atlas of Skin Diseases. (First Part.)

1869.   (*Eleventh Year.*)

41. LANCEREAUX's Treatise on Syphilis. Vol. II.
42. TROUSSEAU's Clinical Medicine. Vol. II.
43. BIENNIAL Retrospect of Medicine and Surgery.
44. ATLAS of Portraits of Skin Diseases. (9th Fasciculus.)

1870.   (*Twelfth Year.*)

45. TROUSSEAU's Lectures on Clinical Medicine. Vol. III.
46. NIEMEYER's Lectures on Pulmonary Consumption.
47. STRICKER's Manual of Histology. Vol. I.
48. ATLAS of Portraits of Skin Diseases. (10th Fasciculus.)

Vol.   1871.   (*Thirteenth Year.*)
49. WUNDERLICH's Medical Thermometry.
50. BIENNIAL Retrospect of Medicine and Surgery.
51. TROUSSEAU's Clinical Medicine.   Vol. IV.
52. ATLAS of Portraits of Skin Diseases.   (11th Fasciculus.)

1872.   (*Fourteenth Year.*)
53. STRICKER's Manual of Histology.   Vol. II.
54. RINDFLEISCH's Pathological Histology.   Vol. I.
55. TROUSSEAU's Clinical Medicine.   Vol. V.
56. ATLAS of Portraits of Skin Diseases.   (12th Fasciculus.)

1873.   (*Fifteenth Year.*)
57. STRICKER's Manual of Histology.   Vol. III.
58. RINDFLEISCH's Pathological Histology.   Vol. II.
59. BIENNIAL Retrospect of Medicine and Surgery.
60. ATLAS of Portraits of Skin Diseases.   (13th Fasciculus.)

1874.   (*Sixteenth Year.*)
61. HEBRA on Skin Diseases.   Vol. III.
62. Von TROELTSCH on Diseases of the Ear.
    HELMHOLTZ on Membrana Tympani, &c.   (In one Vol.)
63. ATLAS of Portraits of Skin Diseases.   (14th Fasciculus.)
64. HEBRA on Skin Diseases.   Vol. IV.

1875.   (*Seventeenth Year.*)
65. BIENNIAL Retrospect of Medicine and Surgery.
66. CATALOGUE of Atlas of Skin Diseases.   (Second Part.)
67. ATLAS of Portraits of Skin Diseases.   (15th Fasciculus.)
68. CLINICAL Lectures by various German Professors.   Vol. I.
69. LATHAM's Works.   Vol. I.

1876.   (*Eighteenth Year.*)
70. SMELLIE's Midwifery, by McClintock.   Vol. I.
71. CLINICAL Lectures by various German Professors.   Vol. II.
72.*CHARCOT's Clinical Lectures on Diseases of the Nervous
    System.   Vol. I.
73. BILLROTH's Lectures on Surgical Pathology.   Vol. I.

1877.   (*Nineteenth Year.*)
74. SMELLIE's Midwifery, by McClintock.   Vol. II.
75. THE Medical Digest, by Dr. Neale.
76. BILLROTH's Lectures on Surgical Pathology.   Vol. II.
77. ATLAS of Illustrations of Pathology.   (Fasciculus I.)

Vol.   1878.   (*Twentieth Year.*)

78. BIBLIOTHECA Therapeutica, by Dr. Waring. Vol. I.
79. SMELLIE's Midwifery, by McClintock.   Vol. III.
80. LATHAM's Works.   Vol. II.
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1879.   (*Twenty-first Year.*)

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1880.   (*Twenty-second Year.*)

86. HEBRA on Diseases of the Skin.   Vol. V.
87. LEXICON of Medical Terms.   (Third Part.)
88. KOCH's Researches on Wound Infection.
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90. CHARCOT's Clinical Lectures on Diseases of the Nervous System.   Vol. II.
91. ATLAS of Illustrations of Pathology.   (Fasciculus III.)

1881.   (*Twenty-third Year.*)

92. SELECTIONS from the Works of Abraham Colles.
93. LEXICON of Medical Terms.   (Fifth Part.)
94. BILLROTH's Clinical Surgery.
95. CHARCOT on Diseases of Old Age.
96. LEXICON of Medical Terms.   (Sixth Part.)
97. ATLAS of Illustrations of Pathology.   (Fasciculus IV.)

1882.   (*Twenty-fourth Year.*)

98. STOKES on Diseases of the Chest.
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Vol.   1883.   (*Twenty-fifth Year.*)

104. ATLAS of Illustrations of Pathology.   (Fasciculus V.)
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1884.   (*Twenty-sixth Year.*)

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1885.   (*Twenty-seventh Year.*)

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1886.   (*Twenty-eighth Year.*)

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1889. (*Thirty-first Year.*)

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VIII.—The Council shall appoint local Honorary Secretaries wherever they shall see fit.

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XIII.—The Council shall lay before the Members at each Anniversary Meeting a Report of their proceedings during the past year, and also an account of the Receipts and Expenditure of the Society; and shall further cause to be printed and circulated among the Members an abstract of such Report and Accounts immediately after such Anniversary Meeting.

XIV.—The annual Accounts of the Receipts and Expenditure of the Society shall be audited by a Committee of three Members, selected at the preceding Anniversary Meeting from among the Members at large.

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XVI.—The local Secretaries shall further the objects of the Society in their respective districts, and shall be in communication with the metropolitan Secretary.

XVII.—The Anniversary Meeting shall be held in the same town as, and at the time of, the Annual Meeting of the British Medical Association, notice of it having been given to all Members at least a week before the day fixed on.

XVIII.—The Members generally shall be invited and encouraged to propose Works, &c., and to make any suggestions to the Council they may think likely to be useful.

XIX.—The Works of the Society shall be printed for the Members only.

XX.—No alteration in the Laws of the Society shall be made, except at a General Meeting. Notice of the alteration to be proposed must also have been laid before the Council at least a month previously.

XXI.—The Council shall have power to call a General Meeting of the Members at any time, and shall also be required to do so within three weeks, upon receiving a requisition in writing to that effect from not less than twenty Members of the Society.

XXII.—All Special General Meetings of the Society shall be held at such place as the Council may appoint.

XXIII.—The Council shall meet at least once in two months, unless by special resolution to the contrary.

GENERAL INFORMATION.

The Subscription is One Guinea annually, to be paid IN ADVANCE. The best mode of sending money is by Cheque, Post-office or Postal Order, payable to Mr. H. K. LEWIS; or by Cheque to the order of the Treasurer, Dr. SEDGWICK SAUNDERS. It is requested that in future all communications in reference to the payment of Subscriptions, or the issue of Books, may be made to Mr. LEWIS, the Society's Agent, and not to the Secretaries.

IMPORTANT NOTICE TO NEW SUBSCRIBERS AND LOCAL SECRETARIES.—New Members who subscribe for the current year and not fewer than three past years at the same time, will be allowed to select volumes from the surplus stock to the value of one guinea without additional payment. The like privilege will be secured each year by any Local Secretary who has the subscriptions of all the members on his list (the number being not less than ten) paid before the end of March for the current year. Arrangements have been made by which new Members can obtain single Volumes, or sets of Volumes, from the Society's stock in hand. Some of the Volumes, of which a larger surplus exists than of others, can be purchased at fixed prices (for which see list). The Society's Agent is empowered to make special arrangements with new Members who may wish to obtain any of the past Volumes.

CARRIAGE, &c.—The Society's Works are supplied free of cost to any address in London, Edinburgh, or Dublin; but the expenses of Carriage to all other places must be borne by the members to whom they are sent. Members are requested to give detailed instructions respecting the mode

by which they wish their Volumes to be forwarded, and also to remember that the Society's responsibility ceases when the Book has been delivered according to the instructions given.   Members residing in the British Isles wishing to receive their Works by post can do so by prepaying the sum of 2s. for the year for postage.

BINDING CASES AND PORTFOLIOS.—The Society's Agent is prepared to supply, at fixed prices, CASES for binding the Lexicon, and PORTFOLIOS for the reception of the Plates of Skin Diseases, and for the Pathological Atlas.

To prevent misapprehensions as regards the punctual issue of each year's series it seems desirable to reprint the following extract from the Report for the year 1882:—

" If the members would kindly understand that the Society's financial year is from January to December, its year of issue from June to June, and that its subscriptions are due in advance, the working of the Society would be much facilitated. From this point of view, the issue of volumes for each succeeding year has always in the past been punctually completed, and probably will be so in the future.   The works promised are issued *for* the year specified, but are not all of them issued *in* it."

The Council will always be glad to receive suggestions from Members, particularly with regard to any recent foreign works which are thought suitable for publication by the Society (*vide* Law XVIII.).   It is requested that such communications be forwarded to the Secretary in the first instance.